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NOVEMBER 1950
VOLUME 62 NUMBER 5

Published Monthly by
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Oct. 30, 1917, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

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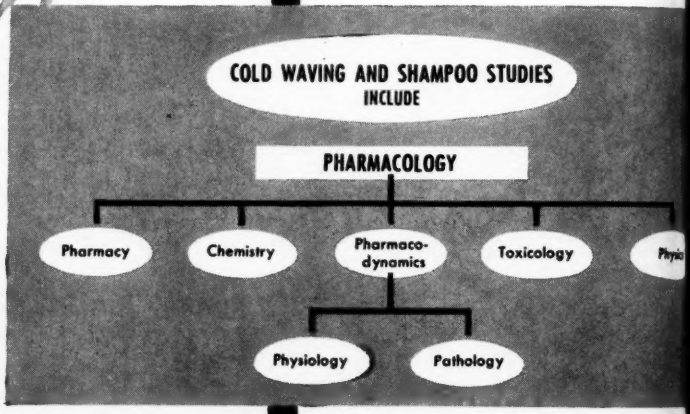

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Archives of Dermatology and Syphilology

VOLUME 62 NOVEMBER 1950 NUMBER 5

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THE DYING SYPHILOLOGIST

President's Address

CHARLES C. DENNIE, M.D.
KANSAS CITY, MO.

THE PRESENT day curriculums of the medical schools do not take into consideration the efficient teaching of the specialties. Instruction in dermatology and syphilology is no exception to the rule. It is perfectly obvious that these divisions must be studied together or they fall together. Internal medicine, surgery and pediatrics are the foundation stones of medicine. The streamlined conveyor belt system of teaching medicine depreciates all the specialties. The trend in medical education is to place all the specialties under the three divisions with the idea that the internist and surgeon will pay attention to certain specialties but still retain their major status. The pediatrician occupies that favorable position where he does not have to pay attention to any one but can use any of the specialties. Whether we like it or not, those in the major divisions of medicine look on us specializing in dermatology and syphilology with ill concealed contempt and regard us as pure externists. They vision us as breaking our hearts over the differential diagnosis of lichen simplex chronicus of Vidal and neurodermatitis. They accuse us of trying to confuse both the patient and the consulting physician with the employment of such terms as lupus miliaris disseminatus faciei acutus, which any Latin student knows describes the pathological conditions, etiological concept, location, form and distribution of the disease and suggests the treatment. They say that the dermatologist and his alter ego the syphilologist treat too many diseases without knowing their cause or origin. They forget that they themselves have seen that day one or more cases of gastric ulcers, hypertension, arthritis, pernicious anemia, myelogenous leukemia and Hodgkin's syndrome and have treated them all without one idea as to the etiological factor.

Is the specialty of dermatology and syphilology worth saving, and what sort of a person practices this art? We believe the physician who practices our art is quite a fellow. Most of the diseases that he treats

Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alberta, Canada, June 19, 1950.

are but reflections of some pathological process within the patient. The man who practices this specialty must know not a little but a great deal about internal medicine. He would make a much better internist than the internist would a dermatologist and could develop into a topnotch internist much more rapidly than an internist could metamorphize himself into a dermatologist.

The dermatologist must be a crack allergist and must be able successfully to manage problems of eczema in children and the skin allergies of the aged. This he does better than either the allergist or the pediatrician. He must be a master on the subjects of infant feeding and the elimination diet for the aged. He is the only one who can manage cutaneous industrial diseases, which comprise 50 per cent of all industrial illnesses.

In World War I and again in World War II, the Army and Navy brass had to learn the hard way that the ordinary physician, no matter how brilliant he was, could not handle the dermatological and venereal problems in the Armed Forces. In the services as in industry, the illnesses that fall into this category compose more than 50 per cent of all diseases encountered. In spite of this experience, the Armed Forces are seeking to eliminate the Marine and the dermatologist, the two most efficient members in their respective fields.

The dermatologist must be a surgeon of sorts and be able to do neat biopsies, perform plastic surgery as the French physicians do, know about the surgical after-care of patients and help the surgeon combat some of the complications.

He must be a good bacteriologist and tissue pathologist. His is a special field in pathological studies. It is a known fact that a topnotch dermatological pathologist can diagnose 90 per cent of cases by looking only at the slide and without a single question whereas the general pathologist makes but two diagnoses, of malignant growths and of acute and chronic dermatitis. The dermatologist is a master of the study of fungous diseases.

He is an expert in the use of roentgen rays and radium in the treatment of skin diseases. His results in treatment of hemangiomas are superior to those of the roentgenologist. His therapeutic results from the use of the roentgen rays are much superior to those of the mere roentgenologist because he recognizes the clinical manifestations of the disease and whether or not the condition will respond to this treatment.

And last, but greatest of all, he is a master psychiatrist. There are more psychiatric problems in the practice of dermatology and syphilology than there are anywhere else in the entire field of medicine except only in the practice of psychiatry itself. A strong psychiatric aspect is encountered in the diagnosis of atopic eczema, neurodermatitis, psoriasis, food

allergies, syphilophobia, minimal suicide or factitious ulcers and other conditions too numerous to mention. The injection of distilled water or of a high dilution of ragweed pollen has exactly the same effect on many allergic patients. The impact of the personality of the successful dermatologist on his patient is beyond measurement. The birth of psychosomatic medicine is due to the unholy mating of the ideas of the psychiatrist and the dermatologist.

In the dermatologist, then, we have a complex medical personality whose technical knowledge and detective abilities in searching for the cause and cure of disease are beyond compare.

We must decide that the division of dermatology and syphilology must remain distinct and independent.

The modern syphilis clinic from which we gain the majority of our statistical facts is a peculiar institution. It has two objects—first, to gather statistics secured by the compilation of the results obtained from the use of penicillin, and, second, to prevent the rest of every other treatment except the administration of penicillin. I am afraid that a great many of these clinics are conducted on the conveyor belt system and that the spirit of dictatorship exists to such an extent that, as in the political realm, it will exclude free thinking. The departments of medicine and surgery in a great many of our institutions have decided that all the specialties shall be subjugated to them except pediatrics, the problem of which is such a peculiar one that its exponents can tell medicine and surgery to back down off their high pedestals. The opinion of the internist is that there is no room for the specialty of dermatology and syphilology and that the internist himself will always be the master mind and know all the answers to problems in dermatology and syphilology except the trifling ones.

The modern syphilis clinic consists of a stock of penicillin, a dark field illuminator and a technician to use it, a nurse to draw blood, an intern to do lumbar punctures, a laboratory technician to run the various serologic tests and a chief to compile the statistics. Based on a review of all the literature that has been compiled since the advent of penicillin, my opinion is that very little has been done in the real diagnosis and study of syphilis except noting the action of penicillin on the patient. Nearly all the reports turn to the serologic results. The writers claim that there is no standard to evaluate clinical results and that the only true standard is the effect that penicillin has on the serologic reactions. I fear that the reason for this stand is the fact that many of these patients are not seen at all or but once only by the physician. The condition of patients certainly can be evaluated by their clinical response. Furthermore, never once do the investigators take into consideration the natural defense of the individual against his disease or the possibility of increasing that resistance. The literature is full of statements that

reinfections occur with great frequency following the administration of penicillin and some authors expressed the opinion that they occur more easily, which observations indicate that the natural immunity to the disease is lowered by the penicillin. Other methods of treatment to raise the immunity of the patient have almost all been discarded. It is penicillin or nothing. The heat boxes are rusting and the malarial strains are dying out all over the country. Eighty per cent of the patients are cured by penicillin alone, but nothing is ever done about the 20 per cent who are not cured. In the practice of syphilology, 80 per cent of the patients with early syphilis are going to receive cures by any modern method of treatment, and anybody can bring about that result whether there is a physician present or not. Skill in medicine of all types, and especially in syphilology, resides in the individual's training and his ability to recognize the different manifestations of the disease. The great fault in the teaching of the principles of syphilology today lies in the fact that there are no longer any expert syphilologists among the young men. The present syphilologists are lost when complications and diagnostic paradoxes occur in the course of the disease of syphilis.

The great mass of knowledge of the disease of syphilis was not studied and compiled by the internist or the surgeon but by many of the old masters who are sitting in this audience today. There are so many of them that I will name none because I could not name them all for want of time.

The pathological processes found in the disease of syphilis are not taught now because they are not known by most young syphilologists. Knowledge of the syphilitic stages guides the therapeutic efforts made to cure and control the disease.

The stage of invasion is that in which Treponema pallidum gains entrance into the body without producing positive changes in the serologic reactions. If penicillin is given before the primary lesion is five days old, practically 100 per cent of the patients are cured. This group represents 0.2 of 1 per cent of all early cases of syphilis.

The stage of infiltration is that in which the body is setting up a defense mechanism against the disease and is pathologically represented by the infiltration of white blood cells around the places that are being attacked. It represents the so-called seropositive stage of syphilis. It is still susceptible to penicillin, but the percentage of cures drops sharply, and the use of penicillin should be followed by other methods of treatment.

The stage of resolution represents clinically the stage of early latency in which penicillin alone is given, but in this stage the effect of the drug on the serologic reactions and clinical course is not satisfactory.

Last, the stage of cicatrization is that in which neither treatment nor the immune forces of the body have defeated the spirochete. This

quiescent stage of syphilis should never be treated by any method, whether with penicillin or antisyphilitic drugs, unless activity makes its appearance.

The medical student is not taught that in the disease of syphilis these pathological processes are the most important part of the understanding of the disease and that after the first flush of the invasion of spirochetes all stages may be taking place at the same time in various portions of the same organ or organs. The Herxheimer reaction, which has jumped into prominence since the use of penicillin, not only proves that penicillin is an effective remedy but also proves that those who are continually bothered with the Herxheimer reaction do not understand it too well. It is not necessary to transform a rather mild man with acute dementia paralytica into a raving maniac or to rupture an aorta by the injudicious use of any dose of penicillin. Time is not so urgent that these patients cannot have some preliminary treatment with the iodides and bismuth preparations and maybe a few heat treatments before the penicillin treatment is begun. The contraindications for the use of penicillin in various diseases are not understood by some of the modern syphilologists because they do not know the pathological changes.

We must conclude, then, that the study of syphilis demands more than a calculating machine and nimble fingers. It requires a brain trained in the recognition of the principles and practices in the treatment of syphilis just as much now as it ever did. The old saying of Osler that "he who knows syphilis in all its phases, knows medicine" is still true.

The differential diagnosis of various skin eruptions is made by the serologist and not by the physician. Determination of the type of neurosyphilis is based on the spinal fluid observations and not on the clinical manifestations. However, there is so much diagnostic meat in the clinical recognition of syphilitic disease that the study of that subject cannot be discontinued.

I have a chart showing the number of hours devoted to the teaching of dermatology and syphilology in various medical schools. The number of hours of teaching is not of much importance, but the quality of that teaching is of the highest importance. Since the advent of penicillin in the treatment of syphilitic diseases, that antibiotic has pierced the heart of the syphilologist and made a field day for the syphilographer. The internist, the surgeon and the obstetrician consider the disease of syphilis of minor importance. Those not trained in the recognition of syphilis in all aspects—and that group includes most of the young teachers in the medical schools—consider the study of this disease as useless. They think penicillin will cure all the cases that can be cured and will wipe the disease out in one more generation. It is true that the number of

syphilitics has been and will be reduced to a great extent, but that does not mean that the disease will ever be entirely wiped out. It will always be a serious problem in medicine.

Furthermore, the assumption that penicillin will cure all the cases that can be cured is an erroneous one and an extremely harmful one. In 20 to 30 per cent of all patients with syphilis except those with seronegative primary syphilis, who are not cured by penicillin, the disease is often susceptible to treatment by other methods, but either these methods have been forgotten or the means of treatment have been discarded. The use of arsenic and bismuth preparations is being depreciated from year to year. The modern therapists have completely forgotten the percentage not cured by penicillin and make practically no effort to investigate the cause, nor do they seek for any better methods of treatment.

Penicillin is not the total answer to the cure of the disease of syphilis. It is the best we have had so far, but I am afraid that the results have been so marvelous in such a large percentage of cases that they have blocked all efforts to a new and better cure for this disease. I was on the American Board for 12 years and resigned from it just as penicillin was coming into its own. Before that time the applicants for certificates were well informed on the subject of syphilis, but since the advent of penicillin the knowledge of this disease among the applicants is deplorable, so much so that the Board has become alarmed and has asked me to read this paper.

The use of penicillin is the direct reason for this bad teaching, not only in syphilology but also in dermatology. The trite statement that the physician injects penicillin into the patient first and then, if it does not cure him immediately, will try to diagnose his disease is true. I see no causes for the bad teaching of syphilology other than the ones I have stated—first, penicillin itself and, second, the influence of the internist who is not a trained syphilologist or dermatologist on this problem. The student must gain a better knowledge of dermatology and syphilology.

The view of the internist that the dermatologist and syphilologist are "externists" has some basis in fact. The members of our specialty are taught to the nth degree about external manifestations but often forget the person who has the disease. The great majority of our certified specialists of the present day do not have a sound foundation in the recognition of diseases that attack the human body as a whole. I would suggest first that the trainee have not only one year's internship work in rotating service but also the equivalent of one year's internship in internal medicine so that he can learn something about the human body besides the manifestations that occur on the outside of it. He must have a knowledge not only of the internal reflections of skin diseases but also

of internal diseases as a whole. This knowledge he does not have at the present time. There is no doubt that the future dermatologist and syphilologist will pay much more attention to internal diseases than does his present day counterpart.

Second, I do not believe that research work on any one problem should occupy very much of the trainee's time before he is certified. He does not now have the time to study the diagnoses and treatments of the basic diseases. I do not mean that he should neglect this field of medicine altogether, but it should comprise only a minimum part of his training. The present teaching of internal medicine is as follows: The chief picks up the chart and looks at data on the chemical condition of the patient's blood and the reports on the various tests that have been performed on the patient before he ever looks at the patient. It remains a fact that the recorded history and physical examination of the patient are still of the greatest importance and should constitute a major part of the study. The teaching of the various technical steps in laboratory studies should not receive much time in the training of the medical student and the time should be reduced to some extent during his internship and residency until he has some idea of what it's all about. I do not think that the medical student during his internship and residency should spend too much time on research work as a problem; he should concentrate only on cases he is investigating, because he does not have enough time or the background to bring a definite research problem to a successful conclusion. This research work should not be discontinued, but the student should wait until he has his feet on the ground medically before he attempts it.

A complete physical examination of every patient should be made unless the person is suffering from a minor ailment. Under the present system of specialism, it is necessary for the specialist to learn his general medicine the hard way, which is a poor way. The young physician must learn that one of the best diagnostic measures is to take off a patient's clothes.

We who are about to die salute you. When the last true syphilologist has assumed an unbending attitude through rigor mortis, may this epitaph be inscribed on his gravestone:

> "Here lies the body of a heretic, condemned to eternal darkness because he dared to teach the principles of his profession against a rising glower of criticism because of his old-fashioned thinking. Long live penicillin!"

SKIN CANCER IN THE AMERICAN NEGRO

H. H. HAZEN, M.D.
AND
C. WENDELL FREEMAN, M.D.
WASHINGTON, D. C.

FOR MANY years Howard Fox [1] and others have repeatedly called attention to the fact that basal cell cutaneous cancers are excessively rare in both dark and light-skinned Negroes. It has also been emphasized that precancerous lesions of the senile and seborrheic wart type are most uncommon. On the other hand, squamous cell carcinomas of both the skin and the mucous membranes are frequently encountered.

The senior author (H. H. H.) has records of 14,100 consecutive cases of skin disease, exclusive of syphilis, observed in the dermatological, surgical and roentgenologic departments of Freedman's Hospital. In addition, the junior author (C. W. F.) has records of 5,000 consecutive patients with skin maladies, again exclusive of syphilis, observed in the same institution or in his private practice. Thus a total of 19,100 consecutive patients have been studied. The results are of some interest, especially because histological examination was performed in practically all instances. A total of 126 cases of cancer were seen, divided as follows:

Basal cell cancers of skin	4
Squamous cell cancers of skin	61
Squamous cell cancers of lip	36
Squamous cell cancers of tongue	17
Squamous cell cancers of genitalia	3
Adenocarcinoma of sebaceous glands	1
Malignant melanoma of skin	1
Kaposi's sarcoma	3

The four basal cell cancers occurred in middle-aged women, none of whom were light mulattos. There were no multiple growths. The sites were the nose, nasofacial fold, nasolabial fold and the back. None of these patients had a keratosis. Only seven precancerous lesions were seen in the 19,000 patients. Curiously enough, all these lesions were

1. Fox, H.: Observations on Skin Diseases in the Negro, J. Cutan. Dis. **26**:67 and 109, 1908.

approximately ½ inch (1 cm.) in diameter when first seen. In three or four instances we have observed small nodular gummas of the face which gave some diagnostic difficulties.

The squamous cell carcinomas were a trifle more frequent in men than in women; all were in persons past 50 years of age. They were located as follows:

Scalp	2
Ear	2
Forehead	2
Cheeks	40
Chin	2
Chest	2
Back	3
Thigh	2
Lower leg	6

The adenocarcinoma of the sebaceous glands occurred on the buttock of a man just 50 years of age. There was no history of a precancerous lesion. When first seen the patient stated that the growth had been present only five months, but it was already 6 inches (15 cm.) in diameter with extensive involvement of the lymph nodes of the groin and pelvis. The cell type of the sebaceous glands was remarkably well preserved.[2]

The one case of malignant melanoma was situated on the sole and was due to the irritation of a flat mole by a nail in the shoe.

Two of the three instances of Kaposi's sarcoma were in men, private patients of the junior author; the third was in a woman seen by the senior author in consultation with Dr. Hayden Kirby-Smith.

The carcinomas of the mucous membranes were largely confined to males. Only one case was of any great interest, a cancer of the upper lip of a very malignant type in a very dark male.[3]

CONCLUSIONS

Basal cell cutaneous cancers and also keratoses are very rare in the Negro race, whereas squamous cell growths are not infrequent. The latter are not infrequent on the lower leg. Malignant melanomas are rare and are most frequent on the sole. Kaposi's sarcomas are probably of about equal frequency in Negroes and white persons.

NOTE.—Since submission of this report, the junior author has seen 2,000 dermatological patients at Freedman's Hospital and in private practice. There were three cases of basal cell carcinoma, all proved by biopsy and all cured by roentgen ray therapy.

2. Hazen, H. H.: Skin Cancer, St. Louis, C. V. Mosby Company, 1916, p. 96.

3. Kerr, H. H., and Hazen, H. H.: Cancer of the Upper Lip in a Pure Negro, J. Cutan. Dis. **29**:321, 1911.

TROPICAL ULCERS

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EASILY demonstrable dermatologic conditions due to a variety of causes are present in about 15 per cent of the routine outpatient clinic and dispensary admissions in seacoast cities of Liberia. This percentage increases in the hinterland until it reaches 43 per cent of the patients in certain rural areas of the Gola Forest. In spite of this relatively high incidence of severe dermatoses, less than 9 per cent of the patients indicate that the skin lesions or associated symptoms are their chief complaints. Even after the examiner has spent considerable time and effort in examinations of the lesions, many of the patients still insist that the lesions are relatively nonimportant parts of their illnesses.

The reactions to tropical dermatoses by Africans differ from those of persons from the temperate zone with similar dermatoses. In the native the condition is often considered relatively insignificant, while the person from the temperate zone recently acquiring the condition becomes rapidly incapacitated. For Allied military personnel operating in the Southwest Pacific during 1944-1945, tropical ulcers were often considered justification for release from further duty in such areas.

The several interrelated factors of etiology are not known for many of these tropical dermatoses. This paper will present some of the laboratory observations for one group of these tropical skin lesions, the so-called tropical ulcers.

The chronic indolent ulceration predominantly occurring on the lower extremities of persons living in tropical climates is generally referred to as a tropical ulcer. Most investigators of tropical ulcers recognize the following contributing etiologic factors: (1) surgical or

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Most of the work for this paper was done while the author was serving as Chief, Laboratory and Medical Research, United States Public Health Service Mission in Liberia, in 1947 and 1948, but some of the observations were begun in 1944 while he was doing research work with a military unit of the Armed Forces in the Western Pacific, in New Guinea, Netherlands East Indies, and the Philippines.

repeated traumatization operations involving injuries to lower extremities, (2) delays in medical care for lesions on the lower extremities, (3) the tropical climate, (4) a lack of proper protein and vitamin intake and (5) the presence of other conditions which reduce resistance.

The current report will deal primarily with tropical ulcers in the native population of Liberia, West Africa. This is a stable populational group with fairly uniform conditions of activity and diet. During the twenty months preceding the writing of this paper the laboratory section of the United States Public Health Service Mission in Liberia made bacteriologic studies on tropical ulcers as observed in the indigenous population in several sections of the Republic. The results of studies on 400 cases are given.

Topography of the Lesions.—The ulcers were solitary in 68 per cent of the cases. Seventy-seven per cent of the lesions were on the lower extremities; 11 per cent were on the buttocks or groin; 5 per cent were on the back, especially in the region of the scapulas; 4 per cent were on the shoulder; 2 per cent were on the upper extremities, and there was 1 case with lesions on the neck, and 1 with lesions on the scalp. The presence of Trichophyton tonsurans, Staphylococcus aureus and a gram-negative rod was demonstrated in the case with the scalp lesions. In 9 per cent of the cases there were several lesions involving two or more of the areas listed in this paragraph.

The Ulcer.—There was considerable variation in the duration, size, shape and depth of the ulcers. In general, however, the duration was between three months and ten years.

The patients with the older ulcers gave histories of several intermittent periods of partial healing followed by softening, extension and inflammatory exacerbations of the ulcer and adjacent tissues. The size varied from 1 to 10 cm. in diameter with a tendency to become stationary after one and one-half to three years. Most of the ulcers were round, but their edges were irregular and slightly elevated above the floor of the ulcer and the adjacent skin. The circulation to the edges was impaired by fibrotic changes in the rim of the ulcers. The depth of the ulcers was chiefly limited by the periosteum or fascial covering of muscles or tendon sheaths. Occasionally large blood vessels and nerves could be seen along the floor of the ulcers. When the ulcers appeared on the fleshy parts of the legs they sometimes extended to a depth of 1 cm. below the skin surface with muscle fascia, periosteum and blood vessels exposed.

In spite of exposure by these eroding ulcerations, clinical osteomyelitis or immobilization of joints over which these muscles or tendons function was rare. There were practically no symptoms of neuritis or

history of hemorrhage from these structures, although the floor of the ulcer and structures first mentioned were often open to the air. Lymphangitis and adenitis were rare.

The appearance of the floor of the ulcers varied with the microbic flora. In general, during the dry season a serosanguineous fluid and pseudomembranes were more frequently present over the ulcer floor, while during the wet season a greater amount of granulation tissue with uneven islands of necrosis was observed over the crater floor. Ulcers that began in the wet season were more serpiginous and phagedenic, with softer borders and a fouler odor, than those that began during the dry season. During the wet season the ulcers were also more painful and tender.

Etiology.—The nonspecific contributory factors of tropical ulcers in this series conformed in general to those previously listed. Some of the more direct instruments of trauma and their relative incidences, as revealed by the history and physical examinations, were thorns, sticks or stones which injured bare feet and legs while the patients were on the jungle trails, in 17 per cent; accidental cuts on legs or feet with working tools or falls or other accidental injuries which persons sustained while at work or play, in 21 per cent; itching and scratching following swimming or wading in mud and water (probably hookworm or Schistosoma larvae penetration), in 6 per cent; dermatitis venenata from some plant the patient encountered while walking in the "bush," in 11 per cent; vesication following contact with caterpillars, in 2 per cent; Tunga penetrans or mite penetration on the legs or about the feet, in 7 per cent; bites of glossinae or tabanids followed by ulceration, in 5 per cent, and trauma following an invasion by Sarcoptes scabiei or trauma at the point of exit of a filaria or dracunculus, in 8 per cent. In about 25 per cent neither the patient nor the examiner could determine the most probable initial traumatic agent.

Most of the patients in our series were young adult male laborers. To a large measure the disease appeared to be related to occupation.

For more than six months out of each year the Liberian native lives on a diet deficient in protein and vitamins, chiefly consisting of rice, cassava, palm oil and plantains. This situation was undoubtedly a factor in the chronicity and poor response to drug therapy. Because the Liberian climate is conducive to sweating, the sweat and salt therein may continue to irritate the crater of the ulcer of the active native whether the ulcer is covered or not.

During the twenty months of this survey, 240 of the 400 cases of tropical ulcers were studied bacteriologically during the hot, humid (rainy) season, while 160 cases were studied during the dry season. The

relative incidences of the various microbes present in ulcers varied with the seasons. The investigation of the microbic flora of each ulcer included the following tests and examinations: gram and methylene blue staining of direct smears taken from the floor of the ulcer and under one edge of the crater rim; plain agar, Loeffler's agar and blood agar plate cultures of the smears taken from the same areas and incubated at 37.5 C. aerobically for twenty-four and forty-eight hours followed by fishing, staining and microscopic studies; corn meal agar and/or Sabouraud's glucose agar plate cultures from the same areas incubated at room temperature for four to ten days, colonies fished and studied microscopically; 25 per cent potassium hydroxide or sodium hydroxide hanging drop suspensions made of scrapings, smears or curettements taken from the ulcer rims or floors and studied microscopically, and, finally, guinea pigs or rabbits given injections in some instances to test the pathogenicity or toxicity of organisms isolated by culture. The microbic flora of the 240 cases studied during the wet season are given in table 1, and those of the 160 cases studied during the dry season are given in table 2. These organisms were listed only when they were present in relatively large numbers in the ulcers.

The determination of the presence of streptococci and diplostreptococci was generally based on morphologic identification since they did not grow well aerobically and anaerobic cultivations were not done. During the wet season occasionally ulcers were observed with spirochetes of the Vincent type present without the fusiform bacilli, while in the dry season the fusiform bacilli may be present without the spirochete in a few cases. Even though tropical ulcers may be considered a clinical entity, the data on microbic flora given in tables 1 and 2 show that the ulcers do not have a sufficiently constant microbic flora to justify a bacteriologic entity.

The four most important groups of micro-organisms from the standpoint of rate of evolution of the ulcer, its erosiveness, the amount of discomfort of the patient and resistance of the condition to treatment were the staphylococci, which on isolation showed necrotizing, staphylotoxic and staphylolytic substances as reflected in intracutaneous rabbit injections; Corynebacterium diphtheriae, as shown by guinea pig inoculation; Bor. vincentii with the fusiform bacilli, ulcers containing which show best healing under local and intravenous neoarsphenamine therapy, and the moniliae, which when present in large numbers in the ulcers produced maceration second only to that of fulminating Staph. aureus infection and showed resistance to several internal medications including penicillin, oxophenarsine (mapharsen®) and the sulfonamides. But when the local application of methylrosaniline chloride (1:100)

TABLE 1.—*The Prevalence and Combinations of Microorganisms Found in Tropical Ulcers During the Wet Seasons**

Staph. aureus or Staphylococcus albus alone	5%
Staph. aureus or Staph. albus and Borrelia vincentii with fusiform bacilli	7%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli, moniliae and diplostreptococci	7%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli and Proteus species	3%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli, diplostreptococci and Corynebacterium species	7%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli, and moniliae	4%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli and sarcinae	4%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli, micrococci and gram-negative rods, either Proteus species or coliform	4%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli, moniliae and Epidermophyton floccosum	2%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli, saprophytic spirochetes, gram-positive bacilli and gram-negative rods	2%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli, diplostreptococci and sarcinae	4%
Staph. aureus or Staph. albus and streptococci or diplococci	3%
Staph. aureus or Staph. albus, saprophytic spirochetes, Corynebacterium species and coliform rods	2%
Staph. aureus or Staph. albus, diplostreptococci, micrococci and Corynebacterium species	6%
Staph. aureus or Staph. albus, moniliae, gram-positive saprophytic rods and Corynebacterium species	2%
Bor. vincentii with fusiform bacilli	8%
Bor. vincentii with fusiform bacilli, Pseudomonas aeruginosa and micrococci	2%
Bor. vincentii with fusiform bacilli, diplostreptococci, Corynebacterium species and coliform rods	7%
Bor. vincentii with fusiform bacilli and sarcinae	4%
Bor. vincentii with fusiform bacilli, diplostreptococci and gram-positive bacilli	6%
Bor. vincentii with fusiform bacilli, saprophytic spirochetes, Corynebacterium species and saprophytic gram-positive bacilli	3%
Saprophytic spirochetes, micrococci, Proteus species and larvae of the Muscidae family	3%
Ps. aeruginosa, Escherichia coli and gram-negative micrococci	3%
Moniliae and sarcinae	2%

* There was a miscellaneous group containing some of the combinations listed and one or more of the following organisms: acid-fast rods in 2 cases, gram-negative vibrios in 4 cases, trichophytons or microsporons in 5 cases, Achorion schoenleini in 1 case, clostridia in 5 cases, fungi of the aspergillus or penicillium genera in 7 cases and blastospores and/or cryptococcus buddings in 4 cases. Many of these were contaminants and probably of no etiologic significance; nevertheless, they were parts of the flora of the ulcer or adjacent tissues.

TABLE 2.—*Prevalence and Combination of Micro-organisms Found in Tropical Ulcers During the Dry Seasons*

Corynebacterium species and aerobic streptococci	5%
Corynebacterium species and Staph. aureus or Staph. albus	17%
Corynebacterium species, Proteus species and micrococci	12%
Corynebacterium species, Staph. aureus or Staph. albus and Bor. vincentii with fusiform bacilli	10%
Corynebacterium species, Staph. aureus or Staph. albus, streptococci and moniliae	5%
Staph. aureus or Staph. albus and gram-positive bacilli	11%
Staph. aureus or Staph. albus, gram-positive bacilli and Proteus species	5%
Staph. aureus or Staph. albus, streptococci and gram-positive bacilli	5%
Staph. aureus or Staph. albus, gram-positive bacilli and saprophytic spirochetes.	5%
Staph. aureus or Staph. albus, streptococci and moniliae	5%
Staph. aureus or Staph. albus and coliform rods	5%
Staph. aureus or Staph. albus, streptococci and coliform rods	2%
Staph. aureus or Staph. albus, Bor. vincentii with fusiform bacilli and gram-negative micrococci	3%
Staph. aureus or Staph. albus and larvae of the Muscidae family	2%
Staph. aureus or Staph. albus and saprophytic spirochetes	3%
Ps. aeruginosa and micrococci	1%
Ps. aeruginosa, coliform rods and gram-negative micrococci	1%
Ps. aeruginosa, E. coli and gram-positive bacilli	1%
Moniliae and Proteus species	1%
Moniliae and micrococci	1%

and/or potassium permanganate (1 : 1000) dressings was added to either of the aforementioned basic medications, the monilia-filled ulcers responded well, as reflected in decreased microbic flora and in rapid healing. A moist environment, when the ulcers were wet and sunlight did not get to them, seemed to potentiate the pathogenicity of moniliae. This result was readily observed during the wet season, while during the dry season when the ulcers were left open the moniliae did not thrive so well in them.

The sulfonamides were the most economical of the four standard basic drugs used in the treatment of these ulcers—viz., penicillin, 500,000 units per week; bismuth subsalicylate, 0.25 Gm. intramuscularly per week; oxophenarsine, 0.045 to 0.06 Gm. intravenously per week, and the sulfonamides, 2 to 3 Gm locally or by mouth per day for ten days. A small amount of diphtheria antitoxin was available during this study, and some of the ulcers with proved toxinogenic C. diphtheriae present were treated with diphtheria antitoxin, injected locally around the ulcer and elsewhere in 10,000 to 40,000 unit amounts as an aid to the once per week 0.25 Gm. intramuscular bismuth subsalicylate injections. The results were better than those with any of the other combinations of treatment in which diphtheria antitoxin was not included. The presence of corynebacteria in the ulcers caused no clinically recognizable condition. Two organisms that are known to elaborate definite antibiotic substances, Ps. aeruginosa and Bacillus subtilis, were occasionally identified in these ulcers. In spite of the possible antibiotic potentials of Ps. aeruginosa, whenever it occurred in an ulcer in combination with coliform or gram-negative rods of the Proteus genus the ulcer was generally very painful and did not heal well under treatment with any of the usual medications mentioned.

COMMENTS

A study of the flora of tropical ulcers is a justifiable part of medical management of the condition. The information obtained therefrom will aid in prescribing a more specific drug for the dominant pathogens, will save man days' loss to industry or to military operations and will reduce the period of hospitalization in severe cases. In ulcers more than 5 cm. in diameter, the average healing time is reduced by two to two and one-half months by the adoption of more specific drugs after determination of the microbic flora rather than the use of the frequently practiced dispensary methods of weekly injections of 0.25 Gm. of bismuth subsalicylate or 0.045 to 0.06 Gm. of oxophenarsine or the sulfonamides locally and by mouth in 2 Gm. amounts per day for ten days.

The use of tyrothricin would also reduce the use of sulfonamides locally and reduce the sensitization of the skin which sulfanilamide often produces on repeated local applications.

Incidentally, the prevalence of corynebacteria in these tropical ulcers in Liberia offers an excellent opportunity for the clinical use of tyrothricin for local application. This antibiotic applied locally would probably make an economical adjunct to the sulfonamides taken internally. Penicillin given by injection is, of course, superior to the other drugs in treatment of the ulcers but was and still is not available in adequate amounts to treat the large number of tropical ulcers in Liberia.

Two organisms that were occasionally identified in these ulcers are known to elaborate definite antibiotic substances which may account for the small number or absence of other micro-organisms known to be present on the skin and in the environment in large numbers. One of these antibiotic micro-organisms is Ps. aeruginosa, which secretes pyocyanine and other substances which are important fungistatic agents against A. schoenleini, Trichophyton gypseum, Candida albicans and certain microsporons and against several bacteria including corynebacteria, streptococci, staphylococci and a Vibrio species occasionally seen in stools and ulceration in Liberia. The other commonly present antibiotic bacterium is B. subtilis, a common organism of the native's work environment of mud and water. The subtilin, bacitracin, bacillin and other antibiotics produced by B. subtilis are surely in some degree responsible for the small number of aerobic streptococci and clostridia found in these ulcers. The eumycin elaborated by B. subtilis is strongly fungistatic and may account for the absence of Malassezia furfur or the small number of Trichophyton concentricum found in tropical ulcers, which develop in the middle of cutaneous rings of pityriasis versicolor or tinea imbricata. Some form of epidermatoplasty is indicated in large ulcers with fibrotic rims, but most attempts at epidermatoplasty in Liberia are failures either because of the poor nutritional state of the donor and recipient or because of the moist, humid, sweaty condition of the skin, which interferes with the skin graft "take."

In Pinkerton's series in South Iran [1] the ulcers hardly ever attacked the young and vigorous. The difference in the type of occupation is undoubtedly a factor. It is of interest to observe that epidermophytoses and epidermophytids are not important agents in the Liberian group, while these infections and their associated "id" reactions were important factors in allied military personnel who acquired tropical ulcers in the South Pacific during World War II.

1. Pinkerton, J. M.: Tropical Ulcer, as Seen in South Iran, and Its Treatment with Penicillin, J. Trop. Med. **50**:243, 1947.

During World War II, I observed the use of elaborate and expensive therapeutic procedures on Allied military personnel with tropical ulcers admitted to the general hospitals in New Guinea as evacuees from the Leyte campaign battlefield during the last months of 1944 and the early months of 1945. These soldiers were given 0.2 cc. of standard triple typhoid vaccine intravenously in 1,000 cc. of an isotonic solution of sodium chloride and/or dextrose solution, or 1.0 cc. of standard triple typhoid vaccine by subcutaneous inoculations for fever therapy, as well as a variety of local treatments including sulfanilamide powder and potassium permanganate soaks or methylrosaniline chloride dressings along with a high protein and vitamin intake. The results were very good, but such a treatment is not practical in Liberia where there are more tropical ulcers than there were in well fed, well clothed Allied soldiers during their periods of tropical operations.

CONCLUSIONS

A study of the microbic flora of 400 cases of tropical ulcers in Liberia is presented. During the rainy season the organisms of the greatest prevalence in the ulcers were Staph. aureus or Staph. albus and Bor. vincentii with the fusiform bacilli. During the dry season the organisms of greatest prevalence in the ulcers were Corynebacterium species and Staph. aureus or Staph. albus. Many of the corynebacteria were proved to be C. diphtheriae by culture and inoculations.

When the microbic flora of tropical ulcers of more than 5 cm. in diameter were determined and more specific therapy given, the average healing time was reduced by two to two and one-half months even when compared with the results with such widely used routine treatments as bismuth subsalicylate and oxophenarsine injections or the oral and local use of sulfonamides when applied indiscriminately as is frequently done in Liberia in tropical ulcer cases.

The Rev. Charles R. Britt, B.D., gave clerical and technical assistance in the preparation of this paper.

SYSTEMIC LUPUS ERYTHEMATOSUS

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"DISSEMINATED" lupus erythematosus still means, to a great many internists and general practitioners, just about what it meant to Moritz Kaposi, who coined the name three quarters of a century ago. Said Kaposi:

> Lupus erythematosus may be . . . developed . . . secondly, as disseminated and aggregated small spots . . . which I call Lupus erythematosus disseminatus et aggregatus. [In this form] . . . hundreds of spots of erythematous lupus become distributed over the trunk, on the flexor and extensor surface of the fingers, on the palm and back of the hand, on the arms, thighs, elbows and knees, both back and front, and, in fact, over almost the whole body . . . accompanied by various local and constitutional symptoms . . . undiscernible in the cases which have a persistently chronic course.[1]

Nearly 25 years later, he was still using the term "disseminatus" in a largely physical sense, for his famous atlas [2] contained plates designated variously as lupus erythematosus "discoides et disseminatus," "disseminatus acutus, bullosus, febrilis," "disseminatus et aggregatus faciei et trunci" and "disseminatus capillitii, faciei, trunci, extremitatum."

Emphasis on the "dissemination" of skin lesions, to the detriment of the importance of constitutional symptoms, soon became apparent. Said Bowen, in 1894:

> The disseminated form occurs when large numbers of small discs appear upon the favorite seats of the disease, as well as other portions of the body. . . . Sometimes an acute febrile invasion takes place, accompanied by articular manifestations and nocturnal headache.[3]

And Pusey, in 1911:

> In rare cases . . . lesions develop rapidly and widely over various parts of the body, and in extreme cases become almost universal. . . . These cases usually

1. Kaposi, M., in Hebra, F., and Kaposi, M.: On Diseases of the Skin, Including the Exanthemata, translated and edited by W. Toy, London, The New Sydenham Society, 1875, vol. 4.

2. Kaposi, M.: Handatlas der Hautkrankheiten, Vienna, W. Braumüller, 1899.

3. Bowen, J. T., in Morrow, P. A.: A System of Genito-Urinary Diseases, Syphilology, and Dermatology, New York, D. Appleton & Co., 1894, vol. 3.

pursue an acute course . . . accompanied by fever, joint and bone pains, and gastrointestinal symptoms.[4]

It has been apparent for a long time now that widely disseminated skin lesions are an inconstant and relatively unimportant feature of "disseminated" lupus erythematosus. Indeed, we have come so far in the direction of that realization that we find an expression in Andrews' text of the following somewhat extreme view:

"[Acute disseminated lupus erythematosus] in spite of its name . . . bears little kinship to the benign disease known as the discoid type of lupus erythematosus. Although called by the same name, they may be completely unrelated. Acute disseminated lupus erythematosus is a systemic disease . . . in which the cutaneous lesions are of relatively little except diagnostic importance, the eruption sometimes even being absent." [5]

This last-mentioned fact has occasioned some dissatisfaction with the word "disseminated." Becker and Obermayer [6] abandoned it altogether in favor of the terms "subacute" (with or without constitutional symptoms) and "acute." The polysyllabic Gallicism *lupo-érythémato-viscerite maligne* made its first appearance in the "Quarterly Cumulative Index Medicus" in 1947, in the title of an article by Lian and others.[7] Translated as "malignant lupoerythematovisceritis," it is handled in the "Index" as indicating a syndrome of Libman-Sacks disease. The popularity of the term in France seems to be increasing. Beare, in Ireland, at the suggestion of W. N. Goldsmith, recently published an article under the title "Malignant Lupus Erythematosus." [8] Michelson suggested the term "visceral lupus erythematosus."

COMMENTS

It seems clear that "disseminated" is a misleading and confusing designation for the many cases of this disease which present few, or no, skin lesions; it is equally misleading and confusing for the occasional case of chronic discoid lupus erythematosus with relatively widespread skin lesions but no constitutional symptoms.

"Subacute" and "acute" would be clear enough to dermatologists, but these terms seem too general and not explicit enough. Moreover,

4. Pusey, W. A.: The Principles and Practice of Dermatology, ed. 2, New York, D. Appleton & Co., 1911.

5. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 3, Philadelphia, W. B. Saunders Company, 1946.

6. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, ed. 2, Philadelphia, J. B. Lippincott Company, 1947.

7. Lian, C.; Siguier, F.; Duperrat, B., and Sarrazin, A.: Malignant Lupo-Erythemato-Visceritis (Nosographic Broadening of Libman-Sacks Disease), Bull. et mém. Soc. méd. d'hôp. de Paris **63**:167, 1947.

8. Beare, J. M.: Malignant Lupus Erythematosus, Brit. J. Dermat. **61**:233, 1949.

there are chronic cases of "disseminated" erythematous lupus; are we to call them "chronic acute lupus erythematosus"?

"Malignant" seems at once too explicit and not explicit enough. It does not take into account the fact that an occasional "disseminated" case may run a relatively benign and chronic course, and it does not specify that more than the skin must be involved in order to justify the name. Many a chronic discoid case, especially if complicated by carcinoma, is so destructive and disfiguring as amply to deserve being called "malignant."

"Visceral" conveys the vital concept of involvement of internal organs, but it suggests an anatomical disturbance (cf. "visceral" metastases) rather than a physiologic one, and it excludes, by implication, the skin. It cannot be claimed in defense of the word that the skin is a viscus, because in that event "visceral" might mean purely cutaneous extent.

"Malignant lupoerythematovisceritis" suffers from the same defects as the two preceding terms; in addition, it seems, to American ears at least, unwieldy. "Libman-Sacks disease" has the double drawback of referring to a special visceral complication which can be diagnosed with assurance only at autopsy and of being as uninformative as any other eponym.

It is submitted that the term "systemic" is a simple, familiar, concise and explicit designation, which says no more, and no less, than we now mean when we say "disseminated" in the clinical (rather than the physical) sense. It indicates skin lesions, visceral lesions and "system" (i. e., reticuloendothelial and hematopoietic) lesions. It can easily be modified by designation of acute, subacute and chronic forms according to both the clinical course and the prognosis. It can hardly be misunderstood.

CONCLUSION

It is suggested that medical writers and medical editors abandon the term "disseminated lupus erythematosus" and use in its place the term "systemic lupus erythematosus."

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LENTIGO SENILIS

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DESPITE an abundant literature devoted to pigmentary disturbances of the skin and to cutaneous neoplasms, scant attention has been directed to the subject of lentigines, and yet these hyperpigmented dermal lesions are very common and occasionally undergo malignant changes. A résumé of current knowledge pertaining to the usual type of lentigo is presented here as an introduction to the special topic of lentigo senilis.

LENTIGO

Lentigines are light to dark brown macules or maculopapules with a smooth surface, usually round, oval or sometimes slightly irregular in shape and varying in size from 1 to 6 or 8 mm. in diameter. Brown [1] showed that newborn infants are free of lentigines. These lesions develop most commonly in the third year or later and increase in number with age up to about 20 years, after which the count gradually decreases. They are most numerous on the face and neck, chest, back and upper extremities and are relatively sparse on the lower part of the trunk, thighs and legs.[2] Although their etiology is unknown, it has been established that lentigines appearing very early in life or in unusually large numbers are often preceded by infections, especially prolonged colds, chronic suppurative sinusitis or bronchiectasis,[1] and that under these circumstances the lesions may vary in number and intensity of pigmentation with the duration and severity of the antecedent infection. Terminology in the field of lentigo is obviously lacking in uniformity,[3] but most

From the Department of Dermatology and Syphilology, University of Michigan Medical School.

1. Brown, E. E.: Lentigines: Their Possible Significance, Arch. Dermat. & Syph. **47**:804 (June) 1943.

2. The Treatment of Pigmented Nevi and Melanomas, in Pack, G. T., and Livingston, E. M.: Treatment of Cancer and Allied Diseases, New York, Paul B. Hoeber, Inc., 1940.

3. Zeisler, E. P., and Becker, S. W.: Generalized Lentigo, Arch. Dermat. & Syph. **33**:109 (Jan.) 1936.

dermatologists concede that lentigines and ephelides (freckles) are completely different entities, despite common usage of the two terms as synonyms. Thirty distinctions between them have been compiled,[1] the most significant of which are noted here: Ephelides first appear later in life (6 to 8 years), are located on exposed surfaces most commonly, increase in number after exposure to sunlight, are a light brown or chamois color, contain no dopa-positive cells, never develop into cancer, do not follow infections and are relatively transitory. In contrast, lentigines appear most commonly for the first time in the third year of life,

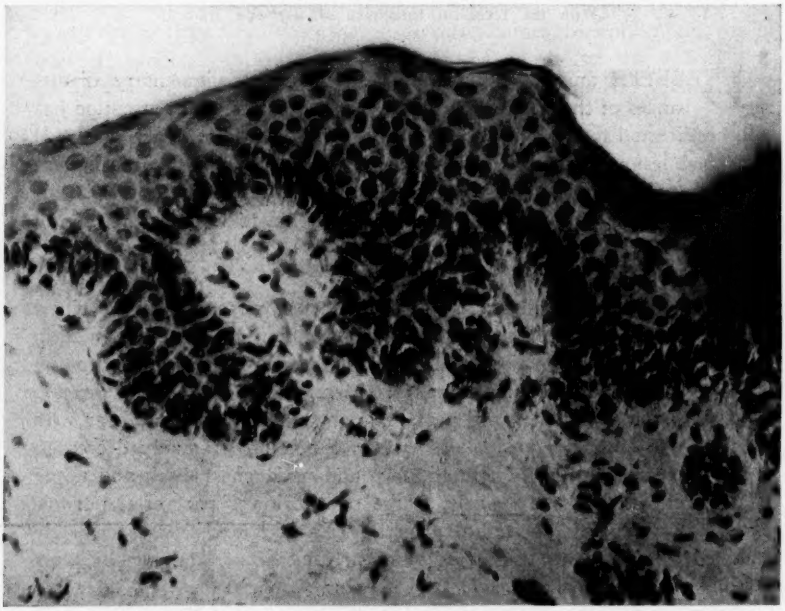

Fig. 1.—Low power view of a section of lentigo showing elongation and proliferation of the rete pegs, occasional clear cells and increased melanin in the basal layer and a few lymphocytes in the upper part of the dermis.

occur on all parts of the body, do not increase in number following exposure to sunlight, are usually dark brown, contain dopa-positive [4] cells as part of a microscopic architecture (fig. 1) which differs considerably from that of ephelides, sometimes undergo malignant changes, are oftentimes more numerous after infections and persist for years.

4. Becker, S. W.; Praver, L. L., and Thatcher, H.: An Improved (Paraffin Section) Method for the Dopa Reaction, Arch. Dermat. & Syph. **31**:190 (Feb.) 1935.

LENTIGO SENILIS

The term lentigo senilis [5] implies the occurrence of lentigines or lentiginoid lesions in senile skin and is a suitable designation for the peculiar pigmented macules occurring on the dorsa of the hands and commonly referred to by the laity as "liver spots." Little specific information is available about these banal lesions, and there are only vague and elusive references to them in the literature.

CLINICAL ASPECTS

Senile lentigines seldom appear before the fourth or fifth decade of life, after which they slowly increase, both in size and number. They

Fig. 2.—Senile lentigines in the usual location. The irregular shape of the lesions is well shown.

start as minute yellowish or light brown macules which enlarge peripherally, sometimes attaining the size of 1 cm. or more in diameter after several years, and are located most commonly on the dorsa of the hands and wrists,[6] less frequently on the face and ankles. Their shape is usually irregular, and many such lesions remain discrete, although occasional confluence is noted. In color they vary from the tawny hue of early lesions to the dark brown or gray-brown of older ones, and their number

5. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939.

6. Miescher, G.; Häberlin, L., and Guggenheim, L.: Spotlike Senile Pigmentations: Their Relation to Melanotic Precancerous Conditions and to Senile Warts, Arch. f. Dermat. u. Syph. **174**:105 (May 15) 1936.

may be few or several dozen (fig. 2). Senile lentigines are common, occurring in approximately 25 to 30 per cent of persons more than 50 years of age. Many very elderly patients are completely free of them, however. They are equally common in both sexes and occur in brunets as well as in those of light or sandy complexion. The lesions are asymptomatic, persist indefinitely and rarely undergo malignant change, so far as can be determined, despite a microscopic picture resembling that of xeroderma pigmentosum and simple lentigo in some respects. The

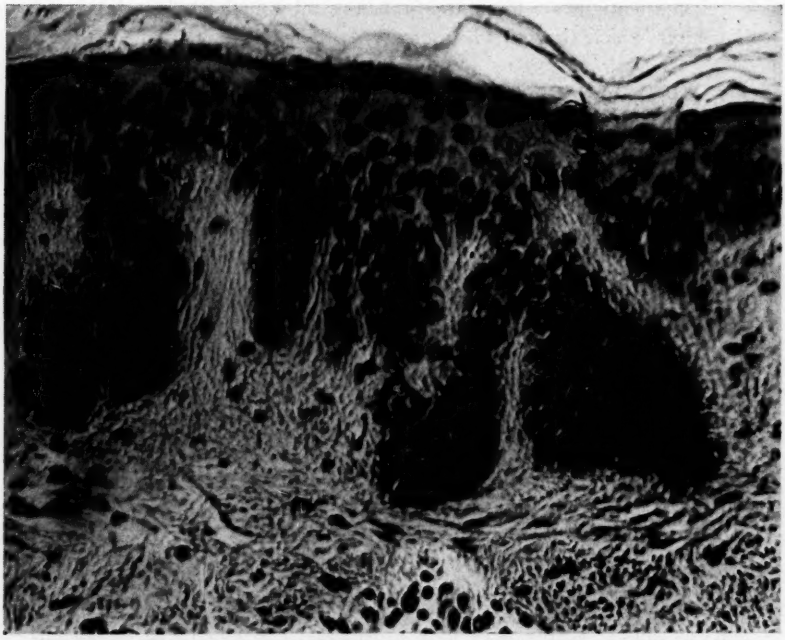

Fig. 3.—The microscopic architecture of lentigo senilis is illustrated here. There is mild hyperkeratosis, and the basal layer is heavily pigmented. Thumblike buds project from several of the rete pegs, and occasional clear cells can be seen. The resemblance to simple lentigo is apparent after comparison with figure 1.

specific etiology of senile lentigines is unknown, although they appear to be a manifestation of the cutaneous aging process, just as are some other pigmentary alterations, and their familial incidence is rather striking. Despite the lay term, "liver spots," and unlike simple lentigo, the lesions of lentigo senilis bear no relationship to the general health of the patient.

HISTOPATHOLOGY

The microscopic architecture of lentigo senilis is distinctive (figs. 3 and 4). There is mild hyperkeratosis and oftentimes a moderate degree of acanthosis. Cells of the stratum mucosum are large, and clear cells are fairly numerous. The basal layer is heavily pigmented, and from many of the rete pegs project eccentric, thumblike buds of varying size not unlike those occurring with xeroderma pigmentosum and simple lentigo. The cells composing these buds are strongly dopa positive

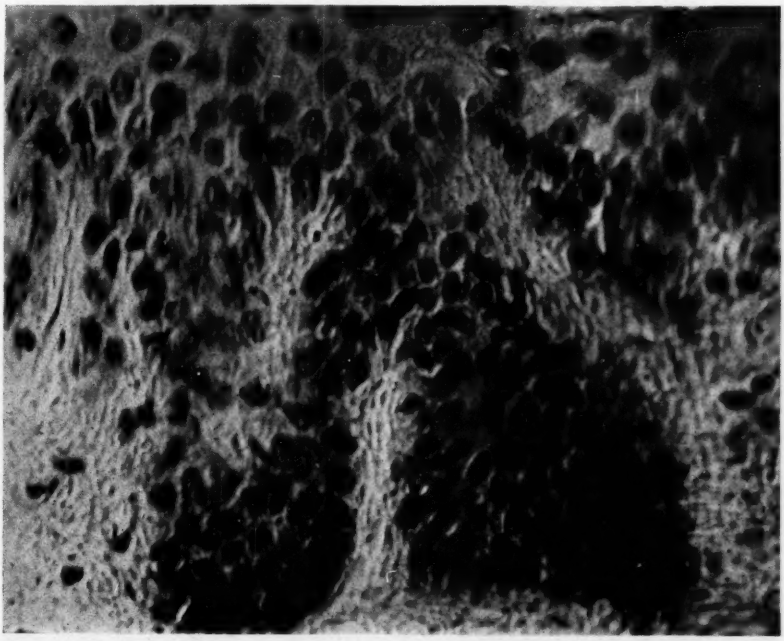

Fig. 4.—High power view of a portion of figure 3, showing details of the rete pegs.

(fig. 5), but the number of mitotic figures is not increased. Many sections reveal a narrow *Grenz* zone beneath which the dermis is atrophic and shows variable degrees of basophilic degeneration. Occasional melanin-laden chromatophores are seen in the dermis, and a mild perivascular lymphocytic infiltrate is usually present.

DIFFERENTIAL DIAGNOSIS

The lesions of lentigo senilis are differentiated from ephelides by their occurrence predominantly on the dorsa of the hands and wrists, the age

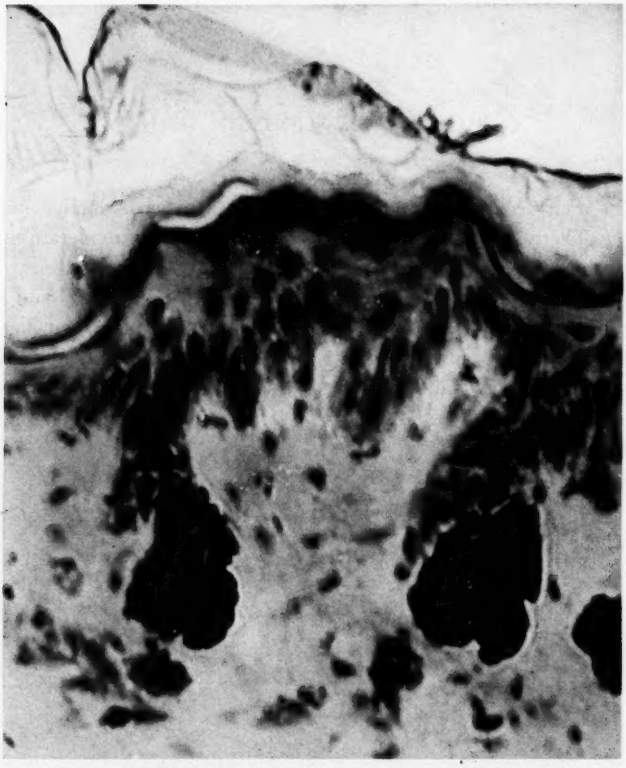

Fig. 5.—A specimen of lentigo senilis showing the positive dopa reaction in elongated and proliferating rete pegs.

Fig. 6.—Microscopic section of a seborrheic keratosis from the dorsum of the hand. The large keratotic cysts are not found with senile lentigines. Clinically, seborrheic keratoses may resemble senile lentigines, but the former are elevated while the latter are macular.

of onset and depth of color and by the fact that sunlight does not influence their development. From simple lentigines they are distinguished by their size, localized distribution and age of onset. Seborrheic keratoses occur at the same sites as and intermixed with senile lentigines and may at times pose a problem in differential diagnosis. The former are usually elevated, though not to the same extent on the hands and wrists as elsewhere, probably because of continued friction at these sites. Also, seborrheic keratoses reveal a microscopic picture which differs considerably from that of lentigo senilis (fig. 6).

TREATMENT

Inasmuch as the lesions of lentigo senilis are benign, treatment is not necessary except as a cosmetic procedure. Most patients want only to be assured that the lesions are not malignant. If treatment is carried out, electrodesiccation and curettage or surgical excision are the preferred methods of therapy.

GRANULOMA INGUINALE AND ITS TREATMENT WITH ORAL AUREOMYCIN

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ALTHOUGH seldom given the publicity of the other venereal diseases, granuloma inguinale probably offers a greater sociologic [1] and treatment problem in the average case than any of the other venereal diseases. Until recent years, there has been no therapeutic agent available which would give satisfactory, sustained and reasonably rapid improvement in these cases.

In 1947 Greenblatt and his co-workers [2] at the University of Georgia reported outstanding results in the treatment of granuloma inguinale with streptomycin. Since that time, numerous authors [3] have reported equally good results with this drug. It was only natural that investigators would further pursue the study of the response of granuloma inguinale to the more recent antibiotics which were being presented to the medical profession. Reports are now beginning to appear in the literature giving the results of the treatment of granuloma inguinale with

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1. Greenblatt, R. B.: Socioeconomic Aspects of Granuloma Inguinale, J. Ven. Dis. Inform. **28**:181-183 (Sept.) 1947.

2. Greenblatt, R. B.; Kupperman, H. S., and Dienst, R. B.: Streptomycin in the Therapy of Granuloma Inguinale, Proc. Soc. Exper. Biol. & Med. **64**:389-390 (April) 1947.

3. Barton, R. L.; Craig, R. M.; Schwemlein, G. X., and Bauer, T. J.: Granuloma Inguinale Treated with Streptomycin: Report of 3 Cases, Arch. Dermat. & Syph. **56**:1-6 (July) 1947. Chen, C. H.; Greenblatt, R. B., and Dienst, R. B.: Streptomycin in the Therapy of Granuloma Inguinale: Report of 100 Cases, J. M. A. Georgia **37**:373-375 (Oct.) 1948. Jacoby, A.; Rosenthal, T., and Sobel, N.: Ambulatory Treatment of Granuloma Inguinale with Streptomycin, Am. J. Syph., Gonor. & Ven. Dis. **33**:76-79 (Jan.) 1949. Zimmerman, R. J., and Smith, G. C.: Granuloma Inguinale—Report of 85 Cases Treated with Streptomycin, J. South Carolina M. A. **44**:267-268 (Aug.) 1948.

aureomycin [4] and chloramphenicol (chloromycetin®),[5] and it appears at present that the results obtainable with aureomycin particularly will exceed those obtained with streptomycin.

Granuloma inguinale was long thought to be endemic only in the tropical regions of the world. To illustrate, one of the titles given to this disease in the past was granuloma inguinale tropicum.[6] Congers and Daniels made the first recorded observations of this disease in Negroes in British Guiana in 1896. Since that time the disorder has been found in many other tropical areas and throughout the southern United States. From Georgia, the Carolinas, Florida, Louisiana, Mississippi and other states have come reports in the past few years describing hundreds of cases of granuloma inguinale. It is therefore likely that the entire southern United States may be considered an endemic area.

Granuloma inguinale begins with a papule or vesicle, followed by a gradual spread by continuity, developing as it spreads into a vividly red-hued granuloma of the skin. Depending on the duration of involvement in each individual, variations may be observed.[7] Ulcerations are seen with reasonably well defined borders showing little or no undermining and the base of the ulcerations still having the granulomatous appearance of the vegetative type of lesion. Many cases show large cicatrized scars with small serpiginous granulomatous areas present. A nodular form has also been observed, which develops as a reddish, soft plaque 1 to 4 cm. in diameter. This is sometimes termed a pseudobubo since it is a subcutaneous infiltration and not a lymph node lesion. We believe that one of the most important points in the differentiation of this disease from other entities involving the external genitalia is the lack of concomitant adenopathy, although this statement is contrary to the observations of Hill, and associates.[8]

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4. (*a*) Greenblatt, R. B.; Dienst, R. B.; Chen, C., and West, R.: Oral Aureomycin in the Therapy of Streptomycin-Resistant Granuloma Inguinale, South. M. J. **41**:1121-1123 (Dec.) 1948. (*b*) Wright, L. T.; Sanders, M.; Logan, M. A.; Prigot, A., and Hill, L. M.: The Treatment of Lymphogranuloma Venereum and Granuloma Inguinale in Humans with Aureomycin, Ann. New York Acad. Sc. **51**:318-330 (Nov. 30) 1948. (*c*) Greenblatt, R. B.; Wammock, V. S.; West, R. M.; Dienst, R. B., and Chen, C. H.: Oral Aureomycin in Therapy of Granuloma Inguinale, Am. J. Syph., Gonor. & Ven. Dis. **33**:593-598 (Nov.) 1949.

5. Greenblatt, R. B.; Wammock, V. S.; Dienst, R. B., and West, R. M.: Chloromycetin in the Therapy of Granuloma Inguinale, J. M. A. Georgia **38**:206-208 (May) 1949.

6. Crocker, H. R.: Diseases of the Skin, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903.

7. Dienst, R. B.; Chen, C. H., and Greenblatt, R. B.: Granuloma Inguinale, Urol. & Cutan. Rev. **53**:537-543 (Sept.) 1949.

8. Hill, L. M.; Wright, L. T.; Prigot, A., and Logan, M. A.: Aureomycin in Granuloma Inguinale, J. A. M. A. **141**:1047-1050 (Dec. 10) 1949.

The sites most frequently found involved are the external genitalia [9] and the perineal region. Perianal involvement is frequently seen but is usually found to be an extension of the process about the external genitalia. We have seen cases involving the lips, the mucous membranes of the mouth, the neck and the cervix uteri and one in which the scalp was involved.

The precise character of the etiologic factor is unknown. The fact that Donovan bodies are demonstrated from smears taken from the lesions suggests these organisms as the possible cause.

CASE MATERIAL

At the South Carolina Public Health Hospital we have treated 17 patients with granuloma inguinale with aureomycin orally, and have been able to follow them for a period of one to seven months. Of this group 14 have been observed from five to seven months after their initial therapy.

All our patients were Negroes, nine female and eight male. Their ages varied between 19 and 59 years; 10 patients were under 35 years of age. None of these were marital or sexual partners so far as could be elicited by interrogation.

Of the total group, seven patients had lesions for a period of six months or less, four for six months to one year, six for a period varying from one year to six years. The size of lesions varied from 2.5 sq. cm. to 169 sq. cm.

Prior to admission to this hospital, four patients had received no form of therapy, four had received an inadequate amount of antimony therapy and nine had received antisyphilitic treatment. None of the patients being reported had received either streptomycin or aureomycin.

DIAGNOSTIC METHODS

The diagnosis of granuloma inguinale in each case was based on both the clinical appearance and the demonstration of Donovan bodies in smears, and dark field examination of all lesions gave negative results. Our procedure for preparing and staining the smears was as follows:

The infected lesion is first cleaned with an isotonic solution of sodium chloride. A small piece of granulation tissue is removed from the lesion by means of a small bone curet. The tissue is then held with a pair of forceps (without teeth), and the under surface is smeared along several glass slides. We have found that macerating the tissue in the forceps during the preparation of the smear induces the flow of additional exudate onto the slide and gives better preparations.

The slides are then dried and stained with either Wright's stain or Giemsa stain. The stock solution of either type is dropped onto the slide until the slide is com-

9. Packer, H.; Turner, H. B., and Dulaney, A. D.: Granuloma Inguinale of the Vagina and Cervix Uteri with Bone Metastases, J. A. M. A. **136**:327-329 (Jan. 31) 1948.

pletely covered. This solution is left on for four minutes, after which the slide is flushed with distilled water and allowed to dry in air. In our hands, we have found that the Donovan bodies are better defined with the Giemsa stain.

DIFFERENTIAL DIAGNOSIS

To anyone who has seen many cases of granuloma inguinale, a differential diagnosis will be obvious in most cases. Other conditions to be considered, however, are ulcerations of a pyogenic nature, tuberculosis of the skin, tertiary syphilids, chancroid, secondary syphilis (such as condylomata lata), carcinoma of the skin and lymphogranuloma venereum. The lack of adenopathy in association with granuloma inguinale should help in the differentiation from syphilis, carcinoma, tuberculosis and chancroid. Lymphogranuloma venereum is a lymphatic disease and usually is not associated with a granulomatous type lesion.

METHOD OF TREATMENT

Treatment, in general, consisted of a total dosage of 25 Gm. of aureomycin, 500 mg. administered orally, in the presence of a registered nurse, every six hours over a 12½ day period. Because of a temporary inadequacy of supply, three persons received less than the total dosage of 25 Gm. of aureomycin; two patients received 24.5 Gm., and one patient received 22.5 Gm. In two cases the daily dose was decreased and the treatment schedule was prolonged to 15 and 16 days, respectively, because of the nausea and vomiting associated with the administration of the aureomycin.

DRUG REACTION

Of the 17 persons treated with oral aureomycin, nausea with or without vomiting occurred in eight. Four of these were able to tolerate the drug without the administration of any antacids, and the symptoms of the other four disappeared when aluminum hydroxide gel (amphogel®) was administered with the aureomycin. We observed no epigastric distress, diarrhea, skin eruptions or fever in our series.

RESULTS AND FOLLOW-UP

Our results have been most encouraging. By the time patients were ready for discharge their lesions showed some degree of healing. In eight patients the lesions were completely healed; in six patients, the majority of lesions were healed; in three patients approximately half of the lesions were healed. One relapse (case 6) was observed, with healing following a second course of aureomycin; the condition remained healed for six months, until the time of writing. One patient (case 7) received a second course of aureomycin when the original lesion had not completely healed one and a half months after his initial course of aureomycin. He remained healed for a period of one month following the second course of aureomycin, until the time of writing.

After a one to seven month follow-up, all the patients showed well formed scar tissue in the sites of the original lesions.

Results of Oral Administration of Aureomycin in Granuloma Inguinale

Case	Race, Sex and Age	Sites of Lesions	Size of Lesions, Sq. Cm.	Duration of Lesions	Total Dose of Aureomycin, Gm.	No. of Days Treated	Drug Reaction	Results on Discharge from Hospital	Follow-Up
1	N, M, 19	Penis	12	6 mo.	24.5	12½	None	Majority of lesions healed	Healed (6½ mo.)
2	N, M, 33	Inguinal, penile, perineal, scrotal regions	48.5	8 mo.	25	12½	Nausea	Majority of lesions healed	Healed (2 mo.)
3	N, M, 32	Perineal region	14	1 yr.	25	12½	Nausea	Majority of lesions healed	Healed (7 mo.)
4	N, F, 36	Vulva, perineal region	169	4 yr.	25	12½	Nausea	Majority of lesions healed	Healed (7 mo.)
5	N, F, 25	Labia majora	8	3 mo.	25	12½	Nausea	Healed on eighth day of treatment	Healed (6 mo.)
6	N, M, 27	Penis	3	1 mo.	24.5	12½	None	Healed	Patient had recurrence of same lesion 25 days after treatment, with positive smears for Donovan bodies; retreated with 25 Gm. of aureomycin over 12½ day period; lesion healed on seventh day (healed 6 mo. following second course of aureomycin)
7	N, M, 36	Penis	38	6 yr.	25	12½	Nausea	Half healed	Lesion of 5 sq. cm. still present 1½ mo. later with smear for Donovan bodies positive; retreated with 25 Gm. aureomycin over 12½ day period; lesion 90% healed following second course of treatment (healed 1 mo. following second course of aureomycin)
8	N, M, 41	Penis	7.5	1 mo.	25	12½	None	Healed on eleventh day	Healed (6 mo.)
9	N, F, 53	Labia majora	7	2 yr.	25	12½	None	Healed on eighth day	Healed (7 mo.)
10	N, M, 31	Penis	17.5	6 mo.	25	12½	None	Half healed	Healed (5 mo.)
11	N, F, 24	Labia majora, inguinal region	25	3 mo.	25	15	Nausea and vomiting	Healed on thirteenth day	Healed (6½ mo.)
12	N, F, 24	Vulva	26	1 mo.	25	12½	Nausea	Healed	Healed (6 mo.)
13	N, F, 59	Post fourchet of external genitalia	2.5	2 mo.	25	12½	None	Half healed	Healed (5½ mo.)
14	N, M, 37	Inguinal, perineal, perianal, oral regions	86	5 yr.	25	12½	None	Majority of lesions healed	Healed (6 mo.)
15	N, F, 47	Perineal region	4	6 mo.	22.5	11	None	Majority of lesions healed	Healed (5 mo.)
16	N, F, 27	Vulva	7	3 wk.	25	12½	None	Healed	Healed (5½ mo.)
17	N, F, 22	Vulva	42.5	1 yr.	25	16	Nausea and vomiting	Healed	Healed (2 mo.)

COMMENTS

Our results confirm the recent observations of Greenblatt and associates.[4c] It appears, however, that certain patients require more intensive and more prolonged treatment than others, regardless of the size of the

original lesions. In our series, two persons (whose lesions were 3 sq. cm. and 30 sq. cm. in size, respectively) required 50 Gm. of aureomycin whereas patients with lesions varying in size from 25 sq. cm. to 169 sq. cm. required only 25 Gm. of aureomycin for complete and sustained healing.

Howard [10] reported that aluminum hydroxide gel interferes with the absorption of aureomycin. The patients in our study who received this antacid and aureomycin concomitantly responded as well as did those who received no aluminum hydroxide gel.

In certain cases, the granulomatous lesions are so extensive as to cause anemia, malnutrition and general debility. The excessive foul odor associated with this type of patient tends to prevent the patient from receiving adequate care from even his own family, and this situation may be considered a factor in the causation of his general debility. Persons with pronounced anemia and malnutrition must be given concomitant supportive therapy such as whole blood transfusions, administration of protein hydrolysates, high vitamin diet and good nursing care to obtain adequate response to specific therapy.

CONCLUSIONS

Aureomycin administered orally is effective in the treatment of granuloma inguinale.

Because of the small number of patients treated and the short follow-up period, no conclusion as to the superiority of aureomycin over any other drug used in the treatment of granuloma inguinale can be made.

SUMMARY

Seventeen persons with granuloma inguinale treated with aureomycin have remained completely healed for one to seven months following treatment with this antibiotic. Of this group, one patient had a relapse and one was re-treated because of incomplete healing.

The use of aluminum hydroxide gel has been reported to reduce absorption of aureomycin, but in this series patients receiving aluminum hydroxide gel showed as much healing on the same dosage schedule as those not receiving the antacid. This observation suggests the possibility that smaller doses of aureomycin than those used in this study may be curative in granuloma inguinale.

10. Howard, R. W.: Aureomycin and Aluminum Hydroxide, Correspondence, J. A. M. A. **141**:938 (Nov. 26) 1949.

APPRAISAL OF THE TOXICITY OF THE GAMMA ISOMER OF HEXACHLOROCYCLOHEXANE IN CLINICAL USAGE

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SINCE the appearance of recent reports by Wooldridge and Cannon and McRae[1] dealing with the use of an ointment containing 1 per cent of the gamma isomer of hexachlorocyclohexane (kwell® ointment, marketed by the Commercial Solvents Corporation) in the treatment of scabies, there have appeared several articles implying that this compound may not be sufficiently safe for clinical usage without further investigation.

These reports have been largely refuted in the light of further investigation. Dr. James G. Sanders, chairman of the Benzene Hexachloride Committee of the National Agricultural Chemicals Association, investigated the published letter of Mobbs[2] and found that the clinical implications contained in that letter could not be substantiated.[3] Furthermore, plant employees in Mobbs's area, engaged in shoveling large amounts of the technical material containing the gamma isomer into fiber containers over a two year period, showed no signs or symptoms of intoxication although no unusual precautions had been observed in preventing skin contact and clothing impregnation.[3]

Studies, observations and reports from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, service of Richard S. Weiss, M.D.

1. (*a*) Wooldridge, W.: The Gamma Isomer of Hexachlorocyclohexane in the Treatment of Scabies, J. Invest. Dermat. **10**:363-366 (May) 1948. (*b*) Cannon, B., and McRae, M.: Treatment of Scabies, J. A. M. A. **138**:557-560 (Oct. 23) 1948.

2. Mobbs, R.: Toxicity of Hexachlorocyclohexane in Scabies, J. A. M. A. **138**:1253 (Dec. 25) 1948.

3. Smith, L.: Personal communication to the authors.

There have been studies investigating the toxicity of the gamma isomer in animals and man.[4] In a report to the Commercial Solvents Corporation, concerning the use of kwell® ointment, Batterman stated as follows:

> A second group of patients were subjects confined to a chronic disease hospital for a multitude of medical conditions. They had relatively normal skin at the time of application of the ointment. Eleven subjects were followed by daily or bidaily application of the ointment over the entire anterior portion of the chest. With the exception of three subjects who had the ointment applied for 8, 11 and 16 trials, the others were studied from 40 to 50 applications. All subjects had received blood counts and urine examinations during the course of the observation. In no instance was there any evidence of toxicity either on the skin or reflected in the blood count or results of urine examinations.[5]

From animal and human experimentation it therefore seems evident that the isomer does possess toxic properties but that toxicity is not induced except in doses many times exceeding those in clinical usage.

Our clinical experiences with the gamma isomer of hexachlorocyclohexane in the treatment of scabies have been extensive and in keeping with the conclusions drawn from the above experimental data. In the clinics of the Barnard Free Skin and Cancer Hospital and the offices of the attending staff more than 300 patients with scabies have been treated with the regular kwell® ointment. The results have been essentially as reported in a previous article,[1a] which showed a cure rate of greater than 95 per cent with a single 24 hour treatment period. In view of the fact that the 1 per cent concentration of the commercial ointment represented an arbitrary figure, we then treated 40 additional patients with an ointment consisting of the same base but with only 0.5 per cent of the gamma isomer. The cure rate with a single treatment period of this half strength ointment was as high as with the full strength ointment previously used.

It therefore seems that this compound is an excellent agent with regard to its therapeutic properties and minimal toxicity. With this in mind we have further investigated it in a controlled series to ascertain its irritant and sensitizing capacities. This portion of the study included the subjecting of 200 volunteers to the "prophetic patch test" as outlined by Schwartz and Peck.[6] These persons were first given patch tests to determine primary irritancy and 10 to 14 days later were again tested to

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4. Horton, R.; Karel, L., and Chadwick, L.: Toxicity of Gamma-Benzene Hexachloride in Clothing, Science **107**:246-247 (March 5) 1948. Slade, R.: The Gamma Isomer of Hexachlorocyclohexane (Gammexane), Hurter Memorial Lecture, Chem. & Indust. **64**:314-319 (Oct. 13) 1945.

5. Batterman, R., Department of Therapeutics, New York University: Personal communication to the authors.

6. Schwartz, L., and Peck, S.: Patch Test in Contact Dermatitis, Pub. Health Rep. **59**:546-557 (April 28) 1944.

determine whether sensitization had occurred. In the 200 subjects so tested none showed a positive reaction. These observations were in keeping with our clinical observations, which revealed a surprising lack of reactions in the large series of patients treated. They were also in agreement with the patch test series of Cannon and McRae.[1b] A single patient, whose case was reported in our previous article,[1a] showed a severe contact type eczematous reaction to the prepared ointment, which reaction, however, was subsequently found to be due to the perfume incorporated into the ointment base.

SUMMARY

On the basis of our own and other recently reported studies it seems clear that the gamma isomer of hexachlorocyclohexane is an excellent therapeutic agent possessing a very wide margin of safety. Furthermore, it seems evident, on the basis of a small series of cases, that the concentration of the gamma isomer may be reduced well below that of 1 per cent without a sacrifice of clinical effectiveness.

CARCINOMA EN CUIRASSE

Primary Lesion in Stomach

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CARCINOMA en cuirasse is the term generally applied to extensive infiltrating plaques resulting from cutaneous metastasis from cancer in other organs of the body. These plaques are usually formed from the coalescence of hard carcinomatous nodules, but at other times pronounced inflammatory reaction is seen, so that many cases have been referred to as carcinoma erysipelotoides. In 1938 Taylor and Meltzer [1] described 38 cases of this inflammatory type of metastasis, all arising from the breast and involving the skin of the chest. Later, in 1941, Reuter and Nomland [2] published a report of a similar case involving the face and neck but with the primary growth in the rectum.

The following case is another example of the inflammatory type of cancer en cuirasse arising from a visceral primary growth.

REPORT OF A CASE

Miss A. S., a retired postmistress, aged 55 years, in September 1947 noticed a small lump in her left axilla. The lump was not painful and was associated with swelling of the anterior axillary fold. Shortly afterward, the patient began to have attacks of pain which radiated from the axilla to the finger tips and the upper arm began to swell. This edema gradually extended down the arm, and by December 1947 the swelling had reached the hand. In January 1948 the swelling at the outer margin of the breast became purplish red and started to spread inward over the breast. This discolored swelling was very hard to the touch but not painful. On March 9, 1948, the patient was admitted to a surgical ward. A diagnosis of chronic streptococcic skin infection was made, and on March 12 parenteral administration of penicillin was started. A daily dose of 200,000 units was given by intramuscular injection. On March 22 there had been no improvement in the condition, and the patient was dismissed on March 26 and instructed to attend as an outpatient at the dermatological department.

From the Department of Dermatology, Royal Infirmary.

1. Taylor, G. W., and Meltzer, A.: Am. J. Cancer **33**:33, 1938.
2. Reuter, M. J., and Nomland, R.: Wisconsin M. J. **40**:196, 1941.

She was seen by one of us (G. H.) on April 20 and immediately admitted to the ward. On admission the patient was well nourished and calm and did not appear to have lost much weight. Her left arm was very swollen and edematous, and there was slight impairment of movement. Spontaneous attacks of acute pain still occurred. Over the left breast, left shoulder and chest wall to below the costal margin on the left side anteriorly the skin was reddish purple, very infiltrated and hard but not painful. The edges of the area were raised and well defined, and from the lower border tonguelike processes extended into the normal skin. A clinical diagnosis of carcinoma en cuirasse was made. The site of the primary lesion was undetermined.

Masses of spheroidal carcinoma cells may be observed in the dilated lymphatic channels of the cutis; × 100.

Previous History.—Until 1941 the patient had enjoyed good health, but in that year she had had a severe nervous breakdown which lasted several months but from which she eventually made a good recovery. Just previous to this nervous upset she had undergone an abdominal operation for visceroptosis and had an uneventful convalescence from this.

Progress.—It was soon obvious that the disease was spreading, and on May 1, 1948, a biopsy specimen was taken from the skin of the chest wall below the breast. This showed the lymphatics of the cutis infiltrated with small masses of spheroidal cell carcinoma (fig.). The neoplasm was not sufficiently differentiated to suggest the site of the primary growth. On May 4 a course of roentgen ray therapy to the chest and neck was started. This was completed on June 9 but produced no

beneficial change in the lesion, which had continued to spread with ever widening processes into the abdomen and outward over the right side of the thorax. There was evidence of roentgen ray erythema around the neck and upper part of the chest, and the irritation from this radiodermatitis was considerable. The patient had an attack of vomiting a week after admission. This was thought to be due to methadone (physeptone®), which had been administered for the pain in her right arm. The pain had gradually become severer and more constant.

On June 8 the patient first complained of difficulty in swallowing and speaking and a choking feeling was experienced over the upper part of the sternum. This gradually increased, and the breathing became rapid and labored for three days and then rather surprisingly began to improve but never returned completely to normal. On June 27 the patient experienced attacks of acute pain in her right arm, and two days later the upper arm began to swell. The edema gradually increased, and on July 4 the edema was massive and the attacks of pain were frequent and severe. The general condition of the patient had gradually deteriorated, and there was superficial ulceration around the lower part of the neck. On July 14 the patient's condition rapidly became worse. She was cyanosed; the pulse rate was increased, and breathing was shallow and rapid. She was restless and semiconscious. These manifestations gradually became severer, and the patient finally passed into a coma and died on July 17.

A postmortem examination was done, and the following report was received: The stomach was small. A diffuse carcinoma was present. This had infiltrated the wall for the whole extent of the lesser curvature and had spread from this line anteriorly and posteriorly toward the greater curvature. The condition approached linitis plastica. Internally the growth had not ulcerated to any extent. Histologically the appearances were those of linitis plastica.

The lungs were partially collapsed, and atrophic emphysema was present. Section revealed the lung parenchyma to be congested and edematous. Histologically metastatic spread along the perivascular lymphatics was a striking feature. The pulmonary tissue in the vicinity was collapsed, and interstitial fibrosis was present.

The breasts were flat, hard and relatively fixed to the underlying fascia. Histologically the lymphatics of the areolar tissue were widely infiltrated with carcinoma deposits.

COMMENT

The clinical diagnosis of carcinoma en cuirasse was easily substantiated by the biopsy from the chest wall. The primary source of the metastatic deposits remained unknown, however, until a postmortem examination was performed and the linitis plastica discovered. In 1937 Gates [3] found that 50 per cent of cutaneous metastases arose from primary carcinoma in the breast and only 15 per cent from a primary tumor of the stomach. In the present case, only a single attack of vomiting gave any clue as to the site of the primary growth.

Suzuki [4] expressed the opinion that death occurs in almost every case within three months of the appearance of dermal secondary lesions arising from the gastrointestinal tract. In this case, however, the progress was much slower and the disease ran a course of seven months or more. This

3. Gates, O.: Am. J. Cancer **30**:718, 1937.
4. Suzuki, N.: J. Cancer Research **3**:357, 1917.

observation is not surprising, as, according to Ormsby and Montgomery,[5] the growth and rate of development of the cutaneous metastasis depends greatly on the primary tumor, which in this case was one of slow development. The failure of the condition to respond to roentgen radiation is not uncommon, and MacKee and Cipollaro[6] stated that the disease is very resistant to roentgen rays.

SUMMARY

A case of carcinoma en cuirasse is reported in which the primary growth was a linitis plastica.

5. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 6, London, Henry Kimpton, 1943, p. 795.

6. MacKee, G. M., and Cipollaro, A. C.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 4, London, Henry Kimpton, 1946, p. 579.

HEMANGIOENDOTHELIOMA OF SKIN WITH METASTASIS TO LIVER, LUNGS AND LYMPH NODES

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HEMANGIOENDOTHELIOMAS are angiomatous tumors with definite evidence of malignant features, which tend to form imperfect capillaries or grow diffusely. They are composed of small channels within groups of endothelial cells, and their characteristic feature is the preponderance of cells over vessels. The name hemangioendothelioma was suggested in 1908 by Mallory.

The tumor may occur on any part of the skin and may be surrounded by satellite lesions. It often ulcerates and bleeds profusely. It is described as not being tender; it is often attached to underlying tissues. The tumor is said to have a characteristic color indicative of blood spaces.

The origin of the hemangiomas and hemangioendotheliomas is essentially the same as that of blood vessels in general. The angioblastic cells from the vascular layer of the mesenchyma lay down solid cords and islands which later unite to form continuous tubes.

The clinical picture of hemangioendothelioma is not distinctive and may be confused with hematoma, angioma and pyogenic granuloma.

Markowitz [1] stated that he considered hemangiomas to be tumors in which the vascular part prevails, while the stroma is rather poor; even if a more cellular stroma is present, it is overshadowed by abundant vessel formation. The same author reported a case of a hemangioma which appeared at the site of an injury and which metastasized to the liver, spleen and iliac bone. In his case the cells did not show anaplasia but presented evidence of invasive and destructive growth.

REPORT OF A CASE

Mrs. M. A., a white woman aged 71 years, entered the hospital on Dec. 22, 1947, complaining of pruritus and chronic swelling of the neck and face.

The present illness had begun in June 1947 with a slowly progressing swelling of the left side of the face, especially of the left cheek and the left mandibular angle.

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School, Dr. Marion B. Sulzberger, chairman, and the Skin and Cancer Unit of University Hospital.

1. Markowitz, B.: Malignant Hemangiomas, Am. J. Clin. Path. **5**:333, 1935.

Some redness accompanied this swelling. The patient applied wet dressings soaked with boric acid, but the condition did not improve. In October 1947 she was examined by her physician, who observed that her entire scalp and face were swollen and erythematous. The eyelids were edematous and closed. In November 1947 the hair started to fall out of the anterior portion of the scalp, which became swollen and red. At the same time the right side of the face began to swell. There was considerable pruritus of the involved area. A few days before admission, the swelling involved the whole face and the eyelids, and the patient could hardly look through the interpalpebral slits. No fever, pain or other discomfort was present. The history showed that at the age of 14 the patient had had erysipelas of the face,

Fig. 1.—Note the dusky color and edema which are most pronounced under the left eye and over the glabella.

which had healed promptly and left no sequelae. However, the patient stated that her face would transitorily swell when "she slept with the windows open" but that the swelling would last for only a day or two. She did not recall any other illness, except that she was "very nervous" and she took some "medicines for her nerves." Two of her sons had died of cancer of the rectum.

The physical examination revealed an elderly woman in no pain or acute distress, apparently in good general health but incapacitated by erythema and swelling of the skin of the face, including the eyelids, making her almost blind (fig. 1.) There was a cone-shaped soft swelling in the region of the glabella, while the swelling of the lower parts of the cheeks and inframandibular region was solid and firm. The skin could not be lifted from the underlying structures. On the left side of

the forehead there was an area suggesting small, closely set nodules, with a granulated appearance. On the anterior part of the scalp there was an area of partial alopecia with a smooth erythematous surface and some scaling. There was no lymphadenopathy except for a slight enlargement of the lymph nodes below the mandibular arches. There were no mucous membrane lesions. The thorax was symmetrical, and expansion was normal. The lungs did not show any pathological signs or symptoms. The heart was very slightly enlarged to the left. No murmurs were audible. The second aortic sound was considerably accentuated. The blood pressure was 185/90. No abdominal abnormality was noticed. A roentgenogram of the chest taken on December 29 showed a slight enlargement of the heart of aortic type with a tubular dilatation of the aortic arch. The lungs were essentially normal. The roentgenogram of the skull showed a slight thickening of the ethmoids, more evident on the left with involvement of the left antrum. Generalized soft tissue thickening was perhaps somewhat more pronounced on the left. The roentgenogram of the abdomen showed advanced osteoarthritic changes of the dorsolumbar portion of the spine.

On Jan. 29, 1948, a skin specimen was taken from the region of the superior carotid triangle and examined in the Department of Pathology (Dr. Maurice Richter, director) of the New York Post-Graduate Hospital (now University Hospital). It showed the following microscopic picture:

"Sections from the skin showed that the dermis was infiltrated by poorly differentiated neoplastic cells which varied greatly in size, were generally elongated and presented round or oval vesicular nuclei with small nucleoli. Many of these cells showed a definite tendency to line spaces, and in some instances they were piled up to form small projections within these spaces (fig. 2). The cytoplasm of these cells was generally eosinophilic, and with a trichrome stain it showed large numbers of fine eosinophilic granules. Mitotic figures were rare. In some instances the proliferation of these neoplastic cells appeared to have originated from the adventitia of larger vessels of venous or arterial type. In spite of the unusual clinical and pathological features it was felt that the growth should be classified as a malignant vascular tumor. A diagnosis of hemangioendothelioma (malignant) of the skin and subcutis of the face was made."

A sternal puncture failed to show any pathological changes. No tumor cells were identified. The blood count was normal. The urine examination showed no abnormality except for one to two red blood cells and occasional white blood cells per high power field. Blood chemistry observations were normal. The patient was given penicillin (9,600,000 units in 12 days), and streptomycin (12 Gm. in six days). Roentgen ray therapy of each side of the face and skull down to the jugular notch was instituted. From January 26 until April 2 the patient was given 3 5/6 skin erythema doses (1 erythema dose—340 r, 100 kv, 2 ma.; target-skin distance, 8 inches [20 cm.]; time, 1 minute 40 seconds; no filtration).

On February 17 a suppurating shallow erosion near the external angle of the left eye, as well as some erosions of the forehead, appeared. From February 23 the patient began to complain of dryness in her mouth and cough and pain in the left side of the chest. A roentgenogram of the chest showed a diminished illumination of the lower 2/3 of the left pulmonary field, varying with change of posture and suggestive of free pleural fluid. The mediastinum was shifted moderately to the right. The right pulmonary field was clear. On March 8, a thoracentesis was performed and 2,100 cc. of a honey-like yellow fluid was removed from the left side of the chest; the specimen was sent to the laboratory for examination. A cell block of the clotted material showed a fibrinous eosinophilic clot containing scattered mononuclear cells. Most of these were small lymphocytes, but larger cells were also

seen. The latter showed eccentric dark-staining nuclei and vacuolated and foamy cytoplasms. Tumor cells were not identified. A smear stained by the Papanicolaou method did not add any further information. On March 18, 1948, 1,200 cc. of straw-colored fluid was removed. This was less sticky and gelatinous than pre-

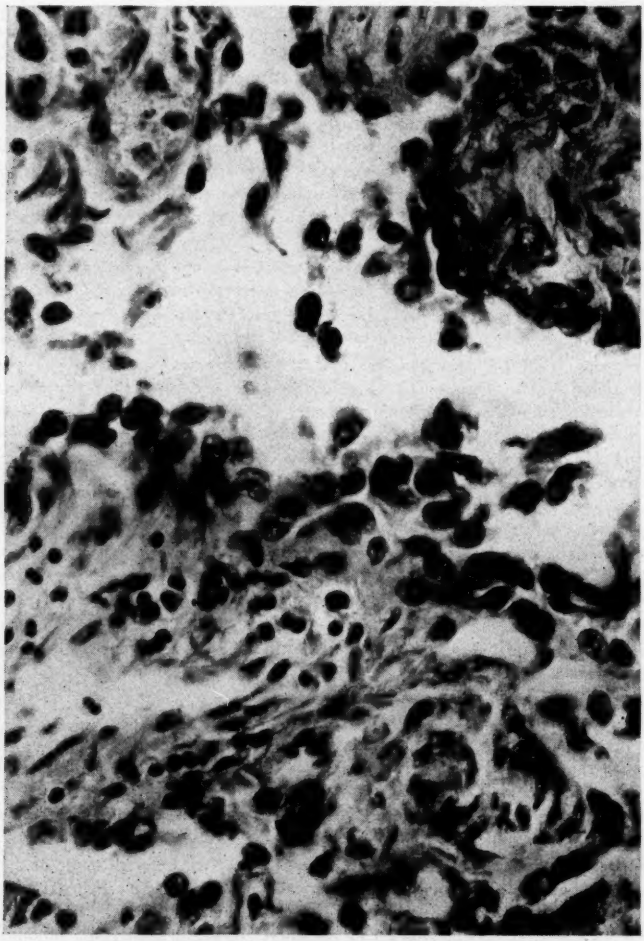

Fig. 2.—Section of skin showing the tendency of the neoplastic cells to "line spaces"; × 551.

viously. A roentgenogram of the thorax done the next day showed a partial resolution of the pleural exudate, and small pea-sized nodules were seen in the midpulmonary field, suggesting metastases. Ten days later a thoracentesis was again performed. This time 2,700 cc. of hemorrhagic fluid was obtained. Bloody

sputum appeared on April 6, 1948, but did not show any pathological cells with Papanicolaou stain. The chest was tapped at eight to 10 day intervals. On April 29, 1,600 cc. of hemorrhagic fluid was removed, but besides red blood cells and lymphocytes no cellular elements were present. The patient felt fairly comfortable until May 4, 1948, when she became dizzy and unconscious and fell into coma. Examination of the blood revealed urea nitrogen of 24 mg. per 100 cc., nonprotein nitrogen of 55 mg. and 3.9 Gm. of total proteins, with 2.5 Gm. of albumin and 1.4 Gm. of globulin.

The patient died the next day without regaining consciousness, on the one hundred and thirty-sixth day of her stay in the hospital.

Autopsy Observations.—The autopsy was performed by Dr. E. Blair of the Department of Pathology of the New York Post-Graduate Hospital.

The left pleural cavity contained 4 liters of serosanguineous fluid as well as numerous fibrous adhesions in its superior portion. The right pleural sac was filled with about 2 liters of purplish creamy material. The right lung was subcrepitant and somewhat firm, a partial atelectasis of all the lobes being indicated. Cut sections of the lung showed a purplish color, especially in the lower lobe. The spleen was essentially normal. The liver surface was purplish tan. Two small circumscribed yellow nodules, each measuring 2 mm. in diameter, were found in the right lobe, and one nodule in the left lobe. No other gross pathological changes were observed, except for the presence of three large stones in the gallbladder and hemorrhages in some lymph nodes (cervical and submental).

The microscopic observations on the tissues taken at the autopsy were as follows:

The pleura showed pronounced lymphocytic infiltrations. Groups of hemosiderin-bearing phagocytes were seen in some areas. Sections from the lower lobe of the left lung showed heavy infiltration by tumor cells throughout. A prominent feature was the perivascular and subpleural infiltration of the tumor. Sections from the right lobe showed perivascular infiltration of tumor cells in several areas. The alveoli were collapsed. Sections of the liver showed several areas of infiltration with cells. Apparently the spread was by way of sinusoids. There was interstitial edema. The hepatic cells generally showed no change. In a submental lymph node the parenchyma had been replaced entirely by tumor tissue. In one portion the bone marrow had been replaced by tumor cells. In some areas these cells "lined spaces" which were filled with blood which exerted such pressure that the tumor cells had become atrophic.

COMMENT

Hemangioendothelioma is a rare neoplasm which may occur at any age, but most of the cases occur in young people. The tumor is highly vascular and usually spreads through either the blood stream or the lymphatics.

Some authors [2] have expressed the opinion that the angioendotheliomas are the connecting link between the benign angiomas and the malignant endotheliomas. Downing and Mallory [3] stated the belief that

2. Pulford, D. S.: Neoplasms of the Blood-Lymph-Vascular System with Special Reference to Endotheliomas, Ann. Surg. **82**:710, 1925.

3. Mallory, F. B.: The Results of the Application of Special Histologic Methods to the Study of Tumors, J. Exper. Med. **10**:575, 1908.

trauma may initiate an arteriovenous communication. The small vessels which are unaccustomed to carry an increased volume of blood would stretch, and this chronic irritation might stimulate the endothelium to proliferate sometimes beyond control. In our case there was no history of trauma but there was a history of erysipelas of the face from which the patient suffered 57 years before the onset of the present condition.

SUMMARY

A case is reported of hemangioendothelioma first noted on the skin of the face. The disease appeared as a solid tumor of the face, diagnosed histologically as hemangioendothelioma, lasted 11 months and terminated fatally. On necropsy metastases to liver, lungs and lymph nodes were found.

ROLE OF PARENTERAL MULTIVITAMIN THERAPY IN THE TREATMENT OF ACNE

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THE EFFECTS of specific vitamins on various skin diseases have been noted by many observers, and the effects of vitamins on the pilosebaceous apparatus have been extensively investigated. Sulzberger and Wolf,[1] in discussing the treatment of acne vulgaris, stated that "the basis of the acne process may be directly attributable to the local effects of the sex hormones on the pilosebaceous apparatus. However, despite the astonishingly rapid progress in endocrinology, the hormonal treatment of acne vulgaris has as yet proved of little value."

The role of vitamin A in the treatment of acne has received wide study following the brilliant report of Frazier and Hu [2] in 1936. Many workers have reported on the beneficial effects of large doses of vitamin A in oil solution. Straumfjord [3] reported that a supplement of 100,000 international units of vitamin A either cured or decidedly improved the condition of 79 of 100 patients suffering from acne, only, however, when the therapy was given over a period of six months. Other workers reported similar observations when vitamin A was used in large doses over prolonged periods. In a critical study of the effects of administering 100,000 units of vitamin A daily in oil, Lynch and Cook [4] reported satisfactory results obtained in 21 out of 45 unselected patients with acne.

More recently, Combes and co-workers [5] reported that 29 of 36 unselected patients with various types of acne showed pronounced

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Dr. Louis Freedman of the U. S. Vitamin Corporation supplied the preparation (vi-syneral® injectable) used in this study.

1. Sulzberger, M. B., and Wolf, J.: Dermatologic Therapy in General Practice, Chicago, The Year Book Publishers, Inc., 1940, pp. 304, 319 and 320.

2. Frazier, C. N., and Hu, C. K.: Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency: A Study of 207 Cases, Arch. Dermat. & Syph. **33**:825 (May) 1936.

3. Straumfjord, J. V.: Vitamin A: Its Effect on Acne, Northwest Med. **42**:219 (Aug.) 1943.

4. Lynch, F. W., and Cook, C. D.: Acne Vulgaris Treated with Vitamin A, Arch. Dermat. & Syph. **55**:355 (March) 1947.

5. Combes, F. C.; Saperstein, R. B., and Distelheim, I.: Vitamin A in Acne Vulgaris, M. Times, New York **77**:473 (Oct.) 1949.

improvement on a daily regimen comprised of the administration of 100,000 units of vitamin A in oil unassisted by other medicinal or special dietary measures.

The developments in the dispersion of oil-soluble vitamin A in aqueous solutions by Freedman [6] have resulted in the development of a new concept in the absorption and utilization of vitamin A. Increased rate of absorption, as shown by peak blood levels of vitamin A, higher liver storage and decreased excretion, have been reported by various investigators. The reports of Lewis and co-workers,[7] Clifford and Weller,[8] Kramer and co-workers [9] and Popper, Steigmann and Dyniewicz [10] demonstrated that the rate of absorption and blood levels of vitamin A are many times higher when the vitamin is administered in the form of aqueous dispersions than when given in oil solutions. On the basis of increased absorption of aqueous vitamin A, Davidson and Sobel [11] used the aqueous dispersion of vitamin A in a multivitamin mixture as a substitute for vitamin A in oil in the treatment of 30 patients with acne. Improvement was noted within two to four weeks, as contrasted with the four to six months necessary when a solution of vitamin A in oil was used. Determination of the serum vitamin A levels of venous blood showed a definitely better absorption of vitamin A with the aqueous form as measured by the vitamin A tolerance tests.

Further effects of the influence of vitamin A deficiency on the pilosebaceous apparatus and its interrelation with the sex hormone changes was studied by Frazier, Hu and Chu.[12] They found that in the presence of a vitamin A deficiency follicular hyperkeratosis occurred most fre-

6. Freedman, L.: Solubilizing of Fat-Soluble Vitamins in Aqueous Media, in abstracts of papers read at one hundred fourteenth meeting, American Chemical Society, Washington, D. C., August 1948.

7. Lewis, J. M.; Bodansky, O.; Birmingham, J., and Cohlan, S. Q.: Comparative Absorption, Excretion, and Storage of Oily and Aqueous Preparations of Vitamin A, J. Pediat. **31**:496 (Nov.) 1947.

8. Clifford, S. H., and Weller, K. F.: The Absorption of Vitamin A in Prematurely Born Infants, with Experience in the Use of Absorbable Vitamin A in the Prophylaxis of Retrolental Fibroplasia, Pediatrics **1**:505 (April) 1948.

9. Kramer, B.; Sobel, A. E., and Gottfried, S. P.: Serum Levels of Vitamin A in Children: A Comparison Following Oral and Intramuscular Administration of Vitamin A in Oily and in Aqueous Mediums, Am. J. Dis. Child. **73**:543 (May) 1947.

10. Popper, H.; Steigmann, F., and Dyniewicz, H.: Treatment of Endogenous Hypovitaminemia in Liver Disease, Proc. Soc. Clin. Research **20**:12 (Nov.) 1947.

11. Davidson, D. W., and Sobel, A. E.: Aqueous Vitamin A in Acne Vulgaris, J. Invest. Dermat. **12**:221 (April) 1949.

12. Frazier, C. N.; Hu, C. K., and Chu, F. T.: Variations in the Cutaneous Manifestations of Vitamin A Deficiency from Infancy to Puberty, Arch. Dermat. & Syph. **14**:1 (July) 1948.

quently at the time of puberty and did not manifest itself as readily in the younger subjects. This relation between the utilization of vitamin A and the endocrine gland changes has been observed in experimental animals. That this process is complex and that there is an interrelation between the effects of vitamins on the pilosebaceous apparatus and the state of the endocrine secretions was ably pointed out by Keddie.[13] Another group implicated in this process are the B vitamins. That the liver is unable to inactivate estrogen in the presence of vitamin B deficiency was shown by Biskind and Biskind.[14] A disturbance in the balance of the sex hormones could result in some liver dysfunction and then in poor utilization of vitamin A. Further, even though dietary intake of vitamins A and B may be adequate, the greater demands by the pilosebaceous apparatus during the adolescent period or at the period of the menstrual cycle may produce a relative inactivation or antagonism sufficient to produce the acne lesion. Hickman, Kaley and Harris [15] stated the conclusion that vitamin A is easily destroyed by the enzymes and oxidants of the intestinal tract and that vitamin E may function as an antioxidant when given by mouth or parenterally at the same time that vitamin A is given. It would seem, therefore, that the addition of vitamin E may be of value in this manner when treating acne vulgaris.

Parenteral injection of vitamin A was found to be superior to the oral use, as shown by the reaction of Dr. Keddie's [13] patient with Darier's disease. Although the absorption of vitamin A from the gastrointestinal tract was not defective, the parenterally injected vitamin A which entered the peripheral circulation appeared to be more effective than that which first passed through the liver. A similar action may take place in patients with acne as well as in those with Darier's disease. Further influences of other vitamins in acne were noted by Sutton and Sutton,[16] who found that a diminished craving for fat had a beneficial effect in acne. Richter [17] also produced this experimentally in rats. Henricksen and Ivy [18] found that viosterol in large doses, 20,000 to 100,000 units, was a

13. Keddie, F.: Use of Vitamin A in the Treatment of Cutaneous Diseases: Relation to Estrogen and the Vitamin B Complex, Arch. Dermat. & Syph. **58**:68 (July) 1948.

14. Biskind, M. S.: Endocrine Disturbances in Gastrointestinal Conditions, Rev. Gastroenterol. **16**:221 (March) 1949.

15. Hickman, K. C. D.; Kaley, M. W., and Harris, P. L.: Covitamin Studies: The Sparing Action of Natural Tocopherol Concentrates on Vitamin A, J. Biol. Chem. **152**:303 (Feb.) 1944.

16. Sutton, R. L., and Sutton, R. L., Jr.: Handbook of Diseases of the Skin, St. Louis, C. V. Mosby Company, 1949.

17. Richter, C. P.; Holt, L. E., Jr.; Barelare, B., Jr., and Hawkes, C. D.: Changes in Fat, Carbohydrate and Protein Appetite in Vitamin B Deficiency, Am. J. Physiol. **124**:596 (Dec.) 1938.

18. Henricksen, J., and Ivy, A. C.: Value of Irradiated Ergosterol in Treatment of Acne Vulgaris, Illinois M. J. **74**:85 (July) 1938.

useful adjunct. Sulzberger and Wolf [1] advocated the use of 150 to 250 mg. of ascorbic acid and the administration of large doses of vitamin D in some cases. Thus, there is good evidence to show an interrelation among vitamins, sex hormones and liver function. That vicious cycles may occur in the interactivity among gastrointestinal function, hormones and vitamins was pointed out by McGavack.[19] He also stressed our lack of knowledge of the specific action of each vitamin in relation to the other vitamins.

If, as has been demonstrated by several observers, large doses of estrogen depress a factor concerned in the absorption and availability of certain vitamins in the body, the addition of vitamins parenterally may be a logical approach to the use of hormone therapy in acne. As has been pointed out earlier, we have no specific for the treatment of acne and, although much physiologic evidence points to the intimate influence of the sex hormones, the results of hormone therapy have been disappointing in the hands of many observers. A combination of parenteral vitamin therapy and hormone therapy should be of value.

CLINICAL STUDY

Forty patients with acne were treated over a period of eight months with intramuscular injections of a parenteral multivitamin preparation [20] in aqueous solution. Twenty-five of these, 18 female and 7 male, remained under treatment for a sufficient period to be included in this report; they ranged in age from 15 to 35 years, and the duration of the acne varied from 18 months to two years. These patients had received previous treatment without improvement. Routine treatment with acne lotions was continued. In two cases roentgen ray therapy was given because of the severity of the disease. Most of the patients were given 2 cc. of the multivitamin solution intramuscularly at weekly intervals. When satisfactory improvement was noted, this interval was increased.

The response to treatment was excellent. Twenty-four patients showed satisfactory improvement, the condition of only one failing to improve during the course of therapy. The rate of improvement in general was much more rapid than I found it to be before using the multivitamin injections. It was in the cystic acnes that the most rapid response was noted. A pronounced regression was noted after three to six injections. This result was in direct contrast to the poor results in cystic acne reported by Combes and associates [5] when large doses of

19. McGavack, T. H., in discussion on Biskind.[14]

20. Vi-syneral® injectable, each 2 cc. of which contains 10,000 units of vitamin A, 1,000 units of vitamin D, 10 mg. of thiamine hydrochloride, 1 mg. of riboflavin, 3 mg. of hydrochloride pyridoxine, 20 mg. of nicotinamide, 50 mg. of ascorbic acid and 2 mg. of alpha tocopherol in aqueous solution containing 4.5 per cent weight per volume of sorethytan monolaurate.

vitamin A were given orally. Several of these patients showing an excellent response to the multivitamin injections had had previous prolonged intensive therapy with local applications, vaccines, hormones and roentgen rays given by competent dermatologists. One girl, aged 16, had a severe cystic acne with conglobate elements. Roentgen ray therapy given when she was 15 had failed to help; oil-soluble vitamin A in large doses and hormone therapy had also failed. She had had intensive treatment for two years. Her response to the multivitamin injections was dramatically rapid. This history was paralleled in a 16 year old boy, after only five injections at weekly intervals. In general, the younger the patient the more rapid was the response. The tendency to relapse after the injections was discontinued was not very great. This observation is in contrast to the results of Davidson and Sobel [11] when a water-soluble multivitamin preparation was administered orally.

SUMMARY AND CONCLUSIONS

The effect of an aqueous multivitamin solution given intramuscularly to 25 patients with acne was studied. The clinical response was excellent. Many cases unresponsive to usual therapeutic procedures showed prompt and consistent progress.

The solution was well tolerated in over 500 injections. In contrast to the effects of oral therapy, there was no pronounced tendency to relapse after the parenteral aqueous therapy was discontinued.

2 East Fifty-Fourth Street.

EXTENSIVE PYODERMATITIS VEGETANS CURED BY ELECTRODESICCATION AND CURETTAGE

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THE ORIGIN [1] of so-called pyoderma vegetans is believed to be a preexisting chronic dermatosis later becoming secondarily infected with Staphylococcus. Treatment usually consists in the application of local antiseptic wet dressings and more recently the use of sulfonamides and antibiotics systemically. The following case report is that of an unusually extensive and severe pyodermatitis vegetans in which the predominating organism was found to be Borrelia refringens. The course of this condition was progressive despite the intensive use of local antiseptics and antibiotics systemically, and not until local destruction by electrodesiccation and curettage did it change favorably.

REPORT OF A CASE

J. H., a Negro aged 29, first noted an ulcerative lesion on the right ankle in September 1944. He was treated as an outpatient for several weeks, but as the lesion progressed in size a local cellulitis developed. The patient was then hospitalized at an Army general hospital. After penicillin therapy for 10 days a generalized urticaria and, later, verrucous type lesions in the groins developed. These were treated locally with complete eradication of the lesions after five months' hospitalization, and the patient was then separated from the Army by certificate of disability with diagnosis of granuloma inguinale and syphilis. Three months later he was admitted to the Veterans Administration Hospital in Columbia, S. C., with a

From the Department of Medicine, Veterans Administration Hospital.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Sutton, R. L., and Sutton, R. L., Jr.: Synopsis of Diseases of the Skin, St. Louis, C. V. Mosby Company, 1942, p. 1144.

generalized bullous eruption associated with some verrucous lesions in the groins and axillas. Microscopic study of a biopsy made at that time was reported as showing nonspecific dermatitis. The patient, improved, left the hospital in two

Fig. 1.—Dermatitis vegetans before treatment.

Fig. 2.—Dermatitis vegetans before treatment.

months; however, the verrucous lesions persisted, and because of an increase in the size of these lesions and the development of considerable foul, purulent exudate he

was again hospitalized in the veterans' section of another Army general hospital, where he was treated for nine months with massive doses of penicillin, weekly doses of oxophenarsine hydrochloride (mapharsen®) and two courses of stibophen (fuadin®), with little or no improvement. He was then transferred, as a private patient, to a university hospital where he was again treated with local applications for several months, with antibiotics, including streptomycin, for two weeks and with stibophen, with no improvement.

Fig. 3.—Dermatitis vegetans six months after electrodesiccation and curettage.

On March 1, 1947, he was transferred to the Veterans Administration Hospital in Columbia, where physical examination revealed an acutely ill, decidedly emaciated, febrile 31 year old Negro who had the appearance of a 50 year old person. The axillas, groins, gluteal folds and anal regions presented large, moist, finger-like, verrucous lesions covered with thickened, offensive, purulent exudate. These areas were extremely tender and bled easily on manipulation (figs. 1 and 2). Both corneas presented numerous white opacities which were thought to be the result of previously reported ulcerative keratitis of unknown causation.

Laboratory work on this admission revealed 3,700,000 red blood cells with 68 per cent hemoglobin and 9,900 white blood cells with a differential count of 46 per cent neutrophils, 60 per cent lymphocytes and 4 per cent eosinophils; the Wassermann reaction of the blood was negative on admission and on numerous reexamina-

Fig. 4.—Dermatitis vegetans six months after electrodesiccation and curettage.

tions; blood chlorides amounted to 438 mg., blood urea nitrogen to 9.5 mg. and blood cholesterol to 130 mg. per 100 cc.; total blood proteins were 4.14 Gm. per 100 cc., with albumin of 2.88 Gm. and globulin of 1.26 Gm. Cultures on Sabouraud's mediums failed to elicit growth.

A biopsy specimen from the right axilla revealed the surface of the resected skin to be covered with stratified squamous epithelium thrown into numerous elongated papillary projections exhibiting pronounced acanthosis and lengthening of the papillae. Some of the tips of the projections were covered with stratum corium containing edematous basket type cells while others showed ulcerations of the epithelium and were covered with exudate made up of polymorphonuclear cells and other leukocytes. The prickle cell layer was thickened. There were numerous polymorphonuclear cells between the epithelial cells. The basal cell layer was intact in all areas and contained abundant brownish pigment. The corium showed distention of the vessels and infiltration with numerous small round cells and polymorphonuclear cells. There were scattered large round cells and occasional eosinophils. The apocrine glands at the base of the lesions appeared normal. The exudate did not extend into the subcutis. No Donovan bodies were found from scrapings of lesions. Dark field examinations and Fontana's staining of a specimen of the fresh material from the surface of the lesions disclosed innumerable spirochetal organisms having the appearance of Bor. refringens.

Therapy consisted of potassium permanganate baths, the administration of stibophen, sedation and routine hospital care without improvement. It was then decided to destroy these verrucous areas by means of fulguration and curettage. This was done in several stages over a period of four months and was accomplished with the use of local, general and spinal anesthesia, as indicated. Postoperative care consisted in blood transfusions given as necessary with general supportive therapy. The fulgurated areas healed with some scar formation which was subsequently treated by the physical therapy department, with the result of considerable loosening of the scar tissue and consequent satisfactory normal range of motion of all the extremities (figs. 3 and 4). The general physical condition of the patient has gradually improved. Red blood cell count and hemoglobin are now entirely normal. The patient is ambulatory, and all lesions are now healed.

SUMMARY AND CONCLUSIONS

An extensive and severe case of pyodermatitis vegetans was successfully treated with local destruction of the lesions by means of electrodesiccation and curettage after failure of these lesions to respond to local antiseptic and systemic therapy consisting in the use of antibiotics and stibophen. Before local destruction was attempted, the patient continued to decline in health and probably would have succumbed to toxemia had resort to this local drastic procedure not been made. The possibility that the patient had pemphigus was eliminated by observing him for 18 months after the local destruction of the lesions. During this period he did not acquire any cutaneous lesions.

Dr. S. L. Zimmerman, Chief of the Medical Service, assisted in the preparation of this paper.

CONTACT DERMATITIS DUE TO SYNTHETIC RESINS IN SHOE LININGS

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DERMATITIS due to materials used in the manufacture of shoes has been reported from time to time. Burgess [1] reported four cases due to leather, canvas or fabrikoid® linings. Shaw [2] reported 22 cases due to such things as tanning chemicals, antimildew compounds, polishes and dyes. Gaul and Underwood [3] recently reported cases due to a wide variety of materials employed in the manufacture of shoes, and Robins [4] recorded cases of dermatitis due to substances used in shoes. No one has, however, stressed the importance of resinous linings as a cause of contact dermatitis. Perhaps the reason is that until recently artificial leathers were simple cellulose nitrate–coated materials. Since World War II a diverse number of resins have been employed as partial linings, particularly in women's shoes.

The purpose of this paper is to indicate the importance of synthetic resins used as partial linings in shoes as a cause of dermatitis of the feet and to point out the probable importance of these substances as a cause of dermatitis of obscure etiology at other sites.

The term "synthetic resins" as employed in this presentation refers to finished compounds as they are employed in shoe linings. Included are basic resins plus all other substances added to modify their physical or chemical characters, such as plasticizers, solvents and pigments.

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Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alberta, Canada, June 21, 1950.

1. Burgess, J. F.: Contact Dermatitis of the Feet, Canad. M. A. J. **47**:27 (July) 1942.

2. Shaw, C.: Dermatitis Due to Shoes, Arch. Dermat. & Syph. **49**:191 (March) 1944.

3. Gaul, E. L., and Underwood, G. B.: Primary Irritants and Sensitizers Used in Fabrication of Footwear, Arch. Dermat. & Syph. **60**:649 (Nov., pt. 1) 1949.

4. Robins, A.: Allergic Dermatitis from Footwear, South African M. J. **17**:345 (Nov.) 1943.

Altogether, 47 proved cases and 29 suspected cases of dermatitis of the feet due to synthetic resins, as defined above, were observed. Proved cases are those in which adequate studies were made so that there is little or no doubt as to the status of resins in the shoe linings as a cause of the dermatitis. Suspected cases are those in which the history, clinical findings and other data suggested resins as a cause but in which complete studies, for one reason or another, were not performed. The latter group of cases is mentioned only to indicate how common resin dermatitis of this type has become. The 76 cases have all been seen during the last four years. Subsequent data is from proved cases.

DESCRIPTION OF CASES

Dermatitis, as seen among this group of patients, had the following characteristics:

The lesions varied from mild erythematosquamous to acute vesiculobullous types.

In general the eruption on the feet was bilateral and symmetrical but patchy in distribution. The location of the patches on the feet varied, and they were found to correspond fairly closely to areas of skin in actual contact with resinous linings when the shoes were being worn.

The commonest areas involved were the dorsa of the feet and toes, most frequently the large toes although the skin of other toes was often involved. The sides of the feet were sometimes affected; the heels and plantar surfaces rarely. The interdigital spaces were not primarily affected, but concomitant ringworm infection was sometimes present in these areas. One patient had a generalized id type of eruption, associated with the lesions on the feet. The bilateral symmetrical patchy distribution of the dermatitis was of great aid in diagnosis.

In adiditon to the lesions on the feet, eight patients had a concomitant bilateral and symmetrical dermatitis on the anterior aspect of the thighs, which corresponded to areas of skin contacted by garter snaps made of a pink synthetic rubber-like material. Three other patients had dermatitis due to adhesive tape, and two others, from elastic. The significance of these observations will be discussed later.

Forty-one of the 46 proved cases were in females. There was nothing significant in the age groups; the youngest patient was 2, and the oldest, 59. The duration of the dermatitis before the patients came under observation varied greatly. It averaged 7.3 months; one patient had had the eruption over five years, and six patients had had it three weeks or less.

ROUTINE PATCH TEST STUDIES

Patch tests with shoe linings were performed in all 47 proved cases. Patients who were suspected of having dermatitis due to resinous shoe linings were instructed to bring in one of each of the shoes they were

Fig. 1.—Shoe showing resinous lining to which patient had strongly positive patch test reaction. Distribution of dermatitis on feet corresponded to areas contacted by the resinous lining.

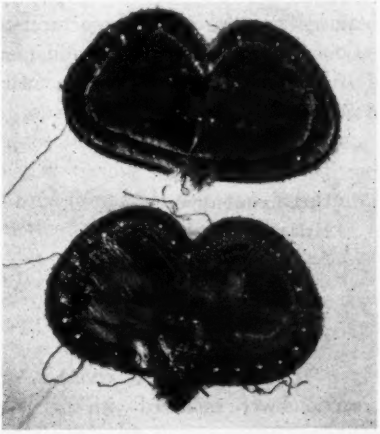

Fig. 2.—Decorative tongues from shoes. Patient gave strongly positive patch test reaction to resin lining. Distribution of dermatitis was limited to areas of feet contacted by tongues.

currently wearing, along with all other articles of footwear. Material was taken from the resinous shoe linings for testing. The linings were usually shiny and of various colors. The degree that shoes were lined with resins varied; quarter to half linings were the commonest. The offending shoes were made by a number of different manufacturers. Patch tests were performed in the usual manner and reactions read at the end of 48 hours. Reactions varied from erythematosquamous to bullous. In 33 of the 47 proved cases there were reactions to the lining of one pair of shoes, while in 14 others there were positive reactions to the linings of two or more pairs. The eight patients who had a concomitant dermatitis on the thighs were tested to the pink rubber. All gave strongly positive reactions.

FOLLOW-UP STUDIES

Patients were instructed to discontinue wearing all shoes to which patch test reactions were positive. After the discarding of offending shoes, healing was usually quite prompt, but this depended somewhat on the degree of chronicity. Other than the aforementioned measure, only simple soothing local applications were employed as treatment.

INVESTIGATIVE STUDIES

Further studies were done on several of the patients in an attempt to find one specific underlying agent responsible for the eruption. Thirteen patients were tested to representative, fully polymerized, unaltered resins as obtained from various manufacturers. In addition to this, tests were also done with 4 per cent formalin (formaldehyde solution U. S. P.) and 10 per cent hexamethylamine. The following plastics were employed:

Phenol-formaldehyde resin
Phenol-furfural resin
Urea-formaldehyde resin
Melamine-formaldehyde resin
Aniline-formaldehyde resin
Vinyl chloride resin
Vinylidene chloride
Polyvinyl butyral
Polyvinyl alcohol

No significant reactions were obtained with this group of substances, it thus being demonstrated that none of these representative basic, well polymerized synthetic resins was responsible for the dermatitis. The study also eliminated formaldehyde as a cause.

Ten other patients were tested to the ingredients of the resinous lining of one pair of shoes to which a patient who wore them gave a

violent bullous patch test reaction. The ingredients were supplied by the manufacturer and consisted of the following substances:

Cellulose trinitrate (nitrocellulose)
Nitrile rubber
Formaldehyde
Butyl alcohol
Tricresyl phosphate
Soybean oil
Two substances of unknown composition
Castor oil
A pigment

No significant reactions were obtained to this group of substances. The patient whose shoe linings contained these materials was not, however, available for patch testing when the materials were received. The tests demonstrated that there is no one common factor responsible for dermatitis due to shoe linings. The formulas vary with the manufacturer. A host of different agents may be present.

SYNTHETIC RESINS AS CAUSE OF DERMATITIS AT OTHER SITES PREVIOUSLY REPORTED

Dermatitis has been reported among workers in the plastics industry, and the principal cause has been formaldehyde and hexamethylenetetramine,[5] used in the manufacture of phenol-formaldehyde or urea-formaldehyde plastics. Schwartz and co-workers [6] reported an outbreak of dermatitis from a resin glue. Six hundred of 800 employees manufacturing this substance were affected. The resinous substance responsible was a phenol-formaldehyde incompletely polymerized molding resin. Schwartz and co-workers pointed out that completely polymerized resins seldom cause trouble; incompletely polymerized ones, often. Synthetic resins used in nail lacquer have frequently been incriminated as a cause of dermatitis,[7] and isolated instances of dermatitis from

5. Lockey, S. D.: Contact Dermatitis Resulting from the Manufacture of Synthetic Resins and Methods of Control, J. Allergy **15**:188 (May) 1944. Cranch, A. G.: Toxicity of Some of the Newer Plastics, Indust. Med. **15**:168 (Feb.) 1946.

6. Schwartz, L.; Peck, S. M., and Dunn, J. E.: Dermatitis from Resin Glue in War Industries, Pub. Health Rep. **58**:899 (June 11) 1943.

7. Sulzberger, M. B.; Rein, C. R.; Fanburg, S. J.; Wolf, M.; Hilliard, M. S., and Popkin, G. L.: Allergic Eczematous Reactions of the Nail Bed, J. Invest. Dermat. **2**:67 (July) 1948. Dobes, W. L., and Nippert, P. H.: Contact Eczema Due to Nail Polish, Arch. Dermat. & Syph. **50**:270 (Oct.) 1944. Keil, H., and Van Dyck, L. S.: Dermatitis Due to Nail Polish: A Study of 26 Cases with the Chief Allergic Components Toluene Sulfonamide Formaldehyde Resin and Related Substances, ibid. **50**:39 (July) 1944.

spectacle frames,[8] nitrocellulose,[9] artificial leather on furniture,[10] resins impregnated in clothing,[11] wrist watch bands,[12] hair lacquers,[13] medications,[14] table cloths,[15] garters [12] and perhaps other things have been reported.

COMMENT

It is apparent from our studies and from observations on 47 cases of dermatitis of the feet in which positive reactions were obtained to patch tests with resinous substances lining shoes, along with observations on 26 patients who had an identical condition in which we were unable to carry out patch test studies, that synthetic resins and their various components as used in shoes are a potent source of dermatitis. This conclusion and the fact that many instances of dermatitis elsewhere than on the feet have been reported due to synthetic resins and their components make it evident that these substances are important cutaneous sensitizing agents. In most instances of proved dermatitis due to these compounds the cause was found because of the clearcut history of exposure to resins and the distribution of the dermatitis. This was true of dermatitis due to hair lacquer pads, spectacle frames, garters and wrist watch bands, for example. It is evident that many obscure cases of dermatitis in which no clearcut history of contact is elicited may be due to these compounds. The use of these substances in commerce is growing by leaps and bounds. They are widely used in laminated woods, as wood finishes on furniture, as furniture-upholstering materials, as varnishes and lacquers, as handles for knives, and in vacuum cleaners, steering wheels, musical instruments, toys, games, sporting goods, wearing apparel, accessories and jewelry, and this fact means that contact with these substances is almost universal.

Synthetic resins as they are employed are highly complex physical chemical mixtures. They are produced by a large number of manu-

8. Berkoff, H. S.: Contact Dermatitis from "Horn-Rimmed" Spectacles: A Report of a Case, Arch. Dermat. & Syph. **38**:746 (Nov.) 1938.

9. Osborne, E. D.; Jordon, J. W., and Campbell, P. C., Jr.: Dermatitis Venenata Due to Nail Lacquer, Arch. Dermat. & Syph. **44**:604 (Oct.) 1941.

10. White, S. J.: Dermatitis from Imitation Leather, Arch. Dermat. & Syph. **45**:1164 (June) 1942.

11. Schwartz, L.: Dermatitis from New Synthetic Resin Fabric Finishes, J. Invest. Dermat. **4**:459 (Dec.) 1941.

12. Zeisler, E. P.: Dermatitis from Elasti-Glass Garters and Wrist Watch Straps, J. A. M. A. **114**:2450 (June 29) 1940.

13. Hollander, A.: Allergic Dermatitis Caused by Hair Lacquer Products, Arch. Dermat. & Syph. **48**:656 (Dec.) 1943.

14. Gaul, L. G., and Underwood, G. B.: The Condensation of Phenol and Formaldehyde to Produce a Sensitizer Unrelated to the Formaldehyde Component, J. Invest. Dermat. **12**:1 (Jan.) 1949.

15. Hitschmann, O. B.: Contact Dermatitis Due to Tablecloth Cover of Vinyl Plastic Fabric, Arch. Dermat. & Syph. **61**:679 (April) 1950.

facturers, and there are at least 17 different classes of synthetic resins, each class of which contains many varieties. At least 400 different plasticizers and solvents, as well as colors and other substances, are employed in modifying the properties of the basic resins.[16] When one considers also that the potency of a basic resin in producing dermatitis depends on the degree of polymerization and that new resins and modifying agents are being constantly introduced, it becomes evident that it is not sufficient in suspected resin dermatitis to test patients to a sample group of basic resins. Any one of several other chemicals present in the resin as employed in the finished article may be the cause of the dermatitis. In order to rule out the diagnosis or establish a case as dermatitis due to synthetic resins, it is necessary to make patch tests with the completed compound to which the skin has been exposed.

It is very difficult to trace down specific ingredients in any one shoe lining. The manufacturers themselves seldom make the resinous linings, and, if they answered inquiries at all, they usually referred to some chemical company which made the coating and from which it was difficult to get a response. It was therefore impossible to determine which basic chemicals present in resinous shoe linings were harmful. It was apparent, from examining linings of shoes, that various synthetic resinous compounds were employed.

Further investigation may aid in determining which resins, plasticizers and pigments are harmful, and elimination of these may reduce the incidence of resin dermatitis.

In the present series it is interesting to note that eight of the 41 females with resin dermatitis of the feet also had a dermatitis due to the pink rubber-like material used as garter snaps and that three others had dermatitis due to adhesive plaster and two others to elastic. Synthetic rubbers, significantly, are used to plasticize other resins (nitrile rubbers), are used in adhesive plaster and may be present in elastic. Sheldon and associates[17] found synthetic rubbers the commonest cause of adhesive plaster tape dermatitis, and Ellis and Siegel[18] reported dermatitis due to synthetic rubber. However, in the present series it was impossible to obtain positive reactions to patch tests with nitrile rubbers in their pure state.

16. Modern Plastics Encyclopedia, New York, Plastics Catalogue Corporation, 1949.

17. Sheldon, J. M.; Hensel, H. M., and Blumenthal, F.: Studies in Adhesive Tape Irritation, J. Invest. Dermat. **4**:295 (Aug.) 1941.

18. Ellis, F. A., and Siegel, J. M.: Allergic Contact Dermatitis Due to Rubber, with Special Reference to Latex, Arch. Dermat. & Syph. **58**:405 (Oct.) 1948.

SUMMARY AND CONCLUSIONS

Data on 47 proved cases of dermatitis of the feet which was due to synthetic resins used in shoe linings are reported. In addition, 29 other suspected cases have been seen.

Dermatitis due to synthetic resins used in shoe linings is commoner in females, varies in severity and in general is bilateral, symmetrical and patchy in distribution, the distribution depending on the degree that the shoes are lined with the resin.

Dermatitis of the feet which is due to synthetic resins is sometimes accompanied with dermatitis at other sites which is due to such substances as synthetic rubbers in garter snaps, elastic and adhesive plaster.

Patch tests performed in the usual manner, employing the resinous linings which contact the areas of dermatitis when the shoes are being worn, are of great diagnostic value.

Elimination of shoes to the linings of which patients give positive patch test reactions usually results in prompt involution of the dermatitis.

The use of a series of synthetic resins for patch tests in cases of suspected resin dermatitis is of little value; patients must be tested to the compounds they actually contact or to all the actual ingredients of the compounds.

The widespread use of synthetic resins in manufacturing and the fact that many isolated instances of resin dermatitis have been reported make it likely that these compounds are an important cause of dermatitis of obscure etiology at sites other than the feet.

ABSTRACT OF DISCUSSION

Dr. Howard J. Parkhurst, Toledo, Ohio: An increasing number of potential irritants and sensitizers are being used in the manufacture of shoes, and we are now indebted to Dr. Jordon for stressing the importance of synthetic resins as a cause of dermatitis of the feet. It is noteworthy that positive patch test reactions were obtained only with the finished materials and not with the individual ingredients. This would seem to indicate that by their combination an irritating compound is formed or that one ingredient may enhance the irritating power of another. And the presence of excessive sweat may be an important factor. In 1941 Dr. Lynch (in discussion on Schwartz[11]: Dermatitis from New Synthetic Resin Fabric Finishes) advised that the finished side of the material be applied to the skin in patch testing because the other side may not contain the irritating substance.

Plastics are widely and increasingly used in our daily life, so that it is practically impossible to avoid contact with them, but in shoes the contact is close and constant during a period of many hours, with perspiration and friction as possible aggravating factors. I should like to inquire how frequently Dr. Jordon encountered hyperhidrosis in his group and also whether many of these patients were going without stockings, as women often do in summer. Only a few men seemed to acquire this dermatitis, and it is possible that these resins are not so widely used in men's shoes.

We may have been missing the diagnosis in some of these cases since the hands may be involved and the eruption may even become generalized. However, the

differential diagnosis usually should not be difficult if we remember that these patches of dermatitis generally conform to the pattern of the shoe linings. Symmetrical lividities might cause some confusion, but the patch test reactions would be negative, and the condition would clear up readily when the hyperhidrosis was checked by astringents, even while the same shoes were worn. Of course, patches of dermatitis due to resins may become secondarily infected with fungi or bacteria, and stasis due to varicose veins may produce stubborn complications.

As a means of prevention it would seem advisable that we try to report all cases of footwear dermatitis to some designated central office where the data could be assembled and classified so that the manufacturers could be notified. Then perhaps less dangerous substances could be substituted in the shoes. Nonallergic footwear will probably never be forthcoming.

Dr. Harry R. Foerster, Milwaukee: I had occasion recently to discuss this subject with a leather chemist who himself had dermatitis of the feet. He pointed out certain interesting observations. The causes of noninfectious dermatitis of the feet are, of course, numerous. As Dr. Jordon has pointed out, one of the chief of these is resin used in linings. However, there are many other sensitizing substances. There are preservatives of various types that are used to protect leather from infection and decomposition, and some of these are mercurials, chrome preparations, phenols and phenolic derivatives and formaldehydes. We know that these chemicals are not infrequent sources of dermatitis on other parts of the body. Leather itself rarely causes dermatitis, but in finishing leather emulsified lacquers are frequently used. These lacquers themselves may provoke dermatitis. The lacquer does not combine with the leather; it simply forms a coating on the surface, and it must be plasticized to make it pliable so that it will not crack. The plasticizers are a variety of organic chemicals, all of which are potential skin irritants.

Another thing called to my attention was that allergic dermatitis from footwear may result from improperly fitted shoes because of the hyperhidrosis that usually results because of pressure and discomfort. As Dr. Parkhurst just stated, sweating macerates the skin and renders it more susceptible to chemical irritation, and the sweat also acts as an absorbent for potential irritants which in the dry form may not provoke dermatitis.

Dr. Jordon has given us an interesting and thought-provoking paper which should stimulate further investigation along these lines.

Dr. Paul A. O'Leary, Rochester, Minn.: A feud is going on between the sole leather industry and the manufacturers of synthetic materials for shoes. It is advisable that a paper of this type undergo a legal survey; also, the deductions drawn must be substantiated by facts and not merely impressions.

Dr. Charles C. Dennie, Kansas City, Mo.: Something must be done for these patients while one is determining the cause of their trouble. My associates and I have found that the unlined brogan tan shoe is the best type of footwear for them.

Dr. Francis A. Ellis, Baltimore: Gaul and Underwood in their paper stressed the importance of the synthetic rubbers used in shoes. From the practical point of view I should like to ask Dr. Jordon, What do you do when a woman has 10 to 15 pairs of shoes? When you take out the lining you certainly destroy the wearing property of that particular pair of shoes. The causative agent appears sometimes to be up under the toe of the shoe; how can one obtain a sample from there without destroying the wearing value of the shoe? The wearing test, of course, can be used in some cases, but the evidence is not usually unequivocal.

Dr. G. Marshall Crawford, Brookline, Mass.: In recent years I have seen an increasing number of these cases, particularly in children. Sometimes it is

possible to incriminate shoe linings or inner soles, but more often I have not been able to prove that the condition was due to these materials and suspected strongly the sneakers that children get into in the spring. When there is a child in whose case I can prove nothing, I try to convince the mother to get him out of sneakers, and then the condition often heals with bland therapy.

One other item is pertinent. For some years there was overemphasis on fungous infections of the hands and feet. More recently contact dermatitis has been placed in greater prominence, but we should still not forget the fungi. It is wise to continue taking routine cultures in at least the more controversial of these foot cases, because fungous infections may be deceiving.

Dr. Richard S. Weiss, St. Louis: My associates and I have recently been contacted by a national association of shoe manufacturers who wanted to know whether we could undertake extensive research on the sensitizing properties of everything that was used in that industry. It seems evident that the shoe industry is alive to the possibility of sensitization, and, in line with Dr. O'Leary's remarks, we should have very competent proof, as there are certainly medicolegal angles.

We are at present testing numerous resin products, plastics and intermediates for one of the great St. Louis chemical houses, and it is a striking fact that we have found very few substances that produced sensitization when judged by the prophetic patch test.

It seems proper, therefore, to surmise that a combination of materials, chemicals and perspiration may be responsible for the reactions observed.

Dr. James W. Jordon, Buffalo: I wish to thank the discussers for their interesting comments. When I prepared this paper, I had no intention of going into all the causes of dermatitis of the feet. I confined myself purely to dermatitis due to synthetic resins present in shoe linings. It is true that there are many other substances present in shoes which may cause dermatitis. We have seen numerous cases in men of dermatitis due to chromium present in shoe uppers. Patch tests with chromium usually gave positive reactions.

Dr. Parkhurst brought up the question of sweating. This is a factor, inasmuch as excess sweat causes substances, particularly plasticizers, to bleed out of the shoe lining. Some resinous coatings contain as much as 50 per cent plasticizer.

Dr. Dennie mentioned lacquered inner soles. Many women's shoes have lacquer on the insoles, but dermatitis from this source is not common, probably because of the thickness of the epidermis on the soles.

Dr. Ellis stated that it was difficult to obtain material from shoes for patch tests because of patients' unwillingness to have their shoes destroyed. It is not necessary, ordinarily, to destroy shoes to obtain material. A small shaving is taken off the suspected lining, and this is used for the test. The shoes are wearable after this procedure. Dr. Ellis also mentioned the importance of fungous infections of the feet as a cause of eczematous dermatitis. I did not wish to imply that infections due to dermatophytes are not an important cause of eczematous dermatitis of the feet. It is usually not difficult to differentiate between dermatitis due to synthetic resins and that due to fungous infection. The former is bilateral and symmetrical, and the latter almost always asymmetrical. Potassium hydroxide examination of material taken from the involved areas is helpful in diagnosis, but this procedure is not always necessary.

CHOLESTEROL FRACTIONATION STUDIES OF THE SERUM OF XANTHELASMA PATIENTS

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THE ASSOCIATION of hypercholesteremia with xanthelasma has been the subject of study by a number of investigators. Although a fair percentage of these cases show definite hyperlipemia and hypercholesteremia, others show values that are well within the accepted normal range. Thus the significance of the concentration of plasma lipids as an etiological factor in the development of these lesions still remains in doubt and additional studies on the subject are needed.

In 1948 Forbes and associates [1] showed that only a small part of the total cholesterol of lyophilized normal plasma or serum is extracted by cold chloroform, while most of the cholesterol of lyophilized serum from nephrotic patients and hypercholesteremic rabbits was thus extracted. This fraction which is thus extracted has been designated the "readily extractable" cholesterol. These investigators expressed the belief that the readily extractable fraction probably represents cholesterol which is either not bound or, at most, very loosely bound with the plasma proteins. It is possible that it may represent the S_f 10-20 class of molecules recently described by Gofman and associates,[2] containing approximately 30 per cent cholesterol by weight but little or no protein. The fraction which is not extracted by chloroform, even in several days, undoubtedly represents cholesterol which is firmly bound with the proteins. Since the extraction of this fraction of cholesterol had never been applied to the serum of persons with xanthelasma it was decided to apply

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Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alberta, Canada, June 21, 1950.

1. Forbes, J. C.; Dillard, G. H. L.; Porter, W. B., and Petterson, O.: Fractionation of Serum Cholesterol, Proc. Soc. Exper. Biol. & Med. **68**:240, 1948.

2. Gofman, J. W.; Lindgren, F.; Elliott, H.; Mantz, W.; Hewit, J.; Strisower, B.; Herring, V., and Lyon, T. P.: Role of Lipids and Lipoproteins in Atherosclerosis, Science **111**:166, 1950.

it in the hope that the results might throw some light on cholesterol metabolism in this condition. All the blood specimens were obtained before breakfast or three or four hours after a practically fat-free breakfast.

PROCEDURE AND METHODS

Serum or plasma, 0.5 cc. is transferred to a ½ ounce (15 cc.) screw-capped bottle capable of withstanding rapid changes in temperature. The serum is then rapidly frozen in an alcohol—solid carbon dioxide mixture and dried for an hour and a half at a pressure of about 0.2 mm. of mercury. Immediately after drying, the bottles are put into a desiccator over calcium chloride. Shortly before extraction, the bottles are tightly capped with a screw cap lined with tin foil and put into a cold room at a temperature of around 5 C. When the temperature of the bottles has dropped to that of the room, 10 cc. of cold chloroform is added to each bottle and the bottles are recapped and shaken at intervals thereafter. At the conclusion of the extraction period, the extracts are filtered cold, taken to the laboratory and analyzed for cholesterol with the use of a previously described procedure.[3]

The fraction designated as "neutral fat plus cholesterol" consists of neutral fat and free and ester cholesterol. A chloroform extract of undried serum obtained by the method of Forbes and Irving[4] is used for the analysis. The serum is absorbed, under specific conditions, on an artificial zeolite (doucil®). This procedure allows complete extraction of the neutral fat and cholesterol by chloroform but prevents extraction of the phospholipids. After filtration, an aliquot of the chloroform extract is evaporated to dryness and its neutral fat and cholesterol content determined by Bloor's oxidation method.[5] Phospholipid phosphorus is determined by the procedure of King[6] as modified by Forbes and Outhouse.[7]

EXPERIMENTAL RESULTS

A few typical results obtained on apparently normal persons are shown in table 1. It will be seen that in practically all cases the extraction is complete at the end of a three hour extraction period. However, in a small percentage of normal subjects there is a definite increased extraction, with increased extraction time. The reason for this divergence from the average normal result is not known, but preliminary work on roosters indicated that it may be related to the neutral fat content of the diet. A high neutral fat content of the diet in these animals usually led to an increased extraction, with increased extraction time.

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3. Gershberg, H., and Forbes, J. C.: Determination of Cholesterol in Whole Blood, Serum or Plasma, J. Lab. & Clin. Med. **27**:1439, 1942.

4. Forbes, J. C., and Irving, H.: Determination of Cholesterol in Whole Blood, J. Lab. & Clin. Med. **16**:909, 1931.

5. Bloor, W. R.: Determination of Small Amounts of Lipid in Blood Plasma, J. Biol. Chem. **77**:53, 1928.

6. King, E. J.: Colorimetric Determination of Phosphorus, Biochem. J. **26**: 292, 1932.

7. Forbes, J. C., and Outhouse, E. L.: Micromethod for Determination of Tissue Lipids, J. Lab. & Clin. Med. **25**:1157, 1940.

TABLE 1.—*Extraction of Cholesterol from Lyophilized Normal Human Serum*

Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extraction, Mg./100 Cc.	Neutral Fat plus Cholesterol, Mg./100 Cc.
227	20	20	25	428
322	30	31	35	511
270	28	25	27	428
226	22	22	20	440
240	22	29	28	504
286	30	22	28	392
215	20	26	21	503
272	32	27	27	551
267	27	42	55	627
233	36	76	102	722

TABLE 2.—*Data on Xanthelasma Patients with Serum Cholesterol Below 300 Mg. per 100 Cc.*

Case No., Sex, Age	Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extraction, Mg./100 Cc.	Neutral Fats plus Cholesterol, Mg./100 Cc.	Phospholipid Phosphorus, Mg./100 Cc.
15, M, 43	269	24	25	34	517	10
16, F, 52	291	34	38	189	470	10
17, F, 46	230	23	28	44	410	11
18, F, 52	160	13	18	21	303	8
19, M, 49	246	26	33	38	458	11
20, F, 55	261	20	25	36	499	9
21, F, 40	294	28	35	57	570	11
22, M, 30	295	19	32	..	504	9
23, F, 54	273	22	29	63	529	12
24, F, 48	282	40	48	83	529	13
29, M, 41	236	35	71	141	600	9
2, F, 44	277	40	78	131	802	..

TABLE 3.—*Data on Xanthelasma Patients with Serum Cholesterol Above 300 Mg. per 100 Cc.*

Case No., Sex, Age	Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extraction, Mg./100 Cc.	Neutral Fats plus Cholesterol, Mg./100 Cc.	Phospholipid Phosphorus, Mg./100 Cc.
1, M, 56	380	232	314	331	790	12
3, F, 61	468	97	401	453	844	18
4, F, 66	453	175	378	392	796	11
5, F, 40	407	44	57	280	797	15
6, F, 54	396	53	179	351	743	8
7, F, 28	343	31	43	214	642	..
8, F, 38	359	40	77	240	689	12
9, F, 56	369	58	149	174	689	11
10, F, 46	352	53	99	262	606	13
11, F, 48	338	72	199	245	630	12
12, M, 42	423	67	206	293	696	15
13, M, 48	316	35	57	95	648	9
29, F, 40	310	46	109	149	689	8

In tables 2 and 3 are shown the results obtained on 25 patients with xanthelasma. Table 2 shows the data on those persons whose total serum cholestrol was below 300 mg. per 100 cc. It will be seen that the three hour extraction (readily extractable) values were roughly normal in all cases but that there was a distinctly greater tendency for the cholesterol extractability to increase, with increased extraction time, than there is in normal individuals. In table 3 are shown the results obtained on subjects with total serum cholesterols of at least 300 mg. per 100 cc. The readily extractable fraction was above normal in nearly all cases, and the tendency for increased extraction, with increased extraction time, was very pronounced. In some cases practically all the cholesterol was extracted by the end of the 72 hour period.

COMMENTS

In 54 per cent of the cases of xanthelasma studied the serum cholesterol values were 300 mg. and above. The three hour value (readily extractable) was roughly normal, below 40 mg., in 12 cases. In 11 of the 13 cases with cholesterols above 300 mg. per 100 cc. the "readily extractable" cholesterol was above 40 mg. per 100 cc. Our results show that a cholesterol value above 300 mg. does not necessarily indicate an abnormality of the readily extractable fraction. Case 1, for instance, had a total cholesterol value of 380 mg., of which 232 mg., or 61 per cent, was extractable in three hours. Case 7 had a total cholesterol of 343 mg., and only 31 mg., or 9 per cent, was extractable in three hours. In table 2 are two cases, no. 24 and no. 2, with a slightly elevated readily extractable fraction with an amount of total cholesterol below 300 mg. It might be stated that we have observed even a greater abnormality in the readily extractable fraction in some serums with cholesterol well below 300 mg. from patients who did not have xanthelasma (see table 8). The tendency for increased extraction, with increased extraction time, was striking in the majority of cases of xanthelasma. This tendency was observed in all cases in which the readily extractable fraction was 31 mg. or above. The values for neutral fat plus cholesterol, on the whole, go hand in hand with the total cholesterol concentration. Although it is impossible to calculate accurately the concentration of neutral fat in the serum, nevertheless, if one assumes a normal free to ester cholesterol ratio, it is evident that the neutral fat concentration could not have been abnormally high, except probably in cases 29 and 2. It may be of interest that in case 2, in which there was the greatest concentration of neutral fat plus cholesterol in relationship to total cholesterol, coronary thrombosis occurred shortly after this test was made.

If we assume 10 mg. per 100 cc. as the upper limits of normal serum phospholipid phosphorus,[8] then 14 out of 23 of our cases showed abnormally high values.

Becker and co-workers[9] in a recent publication reported that the degree of hyperlipemia obtained following the ingestion of a high fat meal was much greater and more prolonged in older people than in young people. The oral administration of either a lipase preparation or polysorbate 80 (tween® 80) to the older persons reduced the hyperlipemic state to that obtained in the young persons. On account of this work, it was decided to administer a pancreatin preparation of good lipase activity[10] to a series of 12 patients with xanthelasma with

TABLE 4.—*Data on Cholesterol Extraction in Xanthelasma Patient before and After Lipase Treatment**

Comment	Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extraction, Mg./100 Cc.	Neutral Fats plus Cholesterol, Mg./.00 Cc.	Phospholipid Phosphorus, Mg./.00 Cc.
Before treatment	338	72	199	249	630	12
Lipase, 4 weeks...	346	36	69	256	708	14
Lipase, 8 weeks...	351	42	77	208	634	12

*This patient, a woman aged 61, remained on her regular diet. The "readily extractable" cholesterol definitely decreased with no clinical improvement in her xanthelasma.

TABLE 5.—*Data on Cholesterol Extraction in Xanthelasma Patient Before and After Lipase Treatment**

Comment	Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extraction, Mg./100 Cc.	Neutral Fats plus Cholesterol, Mg./.00 Cc.	Phospholipid Phosphorus, Mg./100 Cc.
No treatment.....	352	53	99	262	606	13
Lipase, 4 weeks...	368	32	49	62	589	12
Lipase, 12 weeks..	317	24	28	42	553	10

* This patient remained on her regular diet and had taken lipase for three months. The elevated values shown in the table were all reduced to near normal limits. The patient and the referring ophthalmologist expressed the belief that her xanthelasma had partially disappeared. She was continuing on treatment.

hypercholesteremia. The patients were given six 5 grain (0.30 Gm.) enteric-coated pancreatin concentrate tablets before meals. Most of these patients were asked to continue on their regular diet. Some of these showed a reduction in the readily extractable fraction.

The results obtained with four rather typical patients are shown in tables 4, 5. 6 and 7.

8. Thannhauser, S. J.: Lipidoses, in Christian, H. A.: Oxford Loose-Leaf Medicine, ed. 2, New York, Oxford University Press, 1949, vol. 4, pt. 1, p. 214 (55).

9. Becker, G. H.; Meyer, J., and Necheles, H.: Fat Absorption and Atherosclerosis, Science **110**:529, 1949.

10. Supplied by Dr. David Klein, Wilson Laboratories, in the form of 5 grain (0.30 Gm.) enteric-coated, concentrated pancreatin tablets.

TABLE 6.—*Data on Cholesterol Extraction in Xanthelasma Patient Before and After Lipase Treatment**

Comment	Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extract on, Mg./100 Cc.	Neutral Fats plus Cholesterol, Mg./100 Cc.	Phospholipid Phosphorus, Mg./100 Cc.
No treatment.....	343	31	43	214	642	..
Lipase, 4 weeks...	315	28	35	214	761	11
Lipase, 8 weeks...	262	21	27	37	541	8

* This patient remained on her regular diet. Reduction in all values was noticed, but the observation period was too short for any conclusions. There had been no change in the clinical appearance of the patient.

TABLE 7.—*Data on Cholesterol Extraction in Xanthelasma Patient Before and After Lipase Treatment**

Comment	Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extraction, Mg./100 Cc.	Neutral Fats plus Cholesterol, Mg./100 Cc.	Phospholipid Phosphorus, Mg./100 Cc.
Before treatment	468	97	401	453	844	18
Had been taking lipase for 4 weeks	461	45	224	365	706	15
	368	43	88	244	761	13
	507	415	430	427	868	16
	436	64	302	357	779	16
	405	159	338	402	681	10
	399	61	121	241	714	7

* This patient had had xanthelasma for 20 years and had been on a very restricted fat diet for two years on account of gallbladder disease. She took lipase for four months. Both the patient and her family stated the belief that there had been definite regression of the xanthelasma during this period of treatment.

In the entire series of 12 persons on whom we did serum cholesterol determinations we saw no definite change in the cholesterol distribution following lipase administration. No conclusions can be made in this case except that the patient showed decidedly unstable readily extractable cholesterol fraction in her serum and there appeared to be a definite reduction in the phospholipid phosphorus toward the end of the experimental period.

TABLE 8.—*Data Obtained on Subject Without Xanthelasma With Normal Cholesterol but a High Readily Extractable Fraction with Hyperlipemia**

Comment	Total Cholesterol, Mg./100 Cc.	Three Hour Extraction, Mg./100 Cc.	Twenty-Four Hour Extraction, Mg./100 Cc.	Seventy-Two Hour Extraction, Mg./100 Cc.	Neutral Fats plus Cholesterol, Mg./100 Cc.	Phospholipid Phosphorus, Mg./100 Cc.
Before treatment	270	53	74	145	862	12
	263	42	101	142	862	11
Lipase, 12 weeks	234	25	28	50	648	11
	292	172	236	254	1,272	20
	171	18	21	42	531	8
Lipase and very restricted fat diet, 8 weeks	166	21	26	29	473	7
	153	15	15	23	496	7

* After the administration of lipase and a very restricted fat diet, all the values dropped to normal. It might be of interest to mention that this person had been on a restricted fat intake for several years prior to the beginning of this study. In spite of this, the "readily extractable" cholesterol and neutral fat values were decidedly elevated at the beginning of the present study. The subject was on vacation for two weeks prior to taking the fourth blood sample, and the fat content of his diet was not severely restricted during that period. This fact probably explains the very high "readily extractable" value and hyperlipemia observed for that sample.

SUMMARY

Cholesterol fractionation studies on lyophilized serum from xanthelasma patients showed an abnormal cholesterol distribution in the majority of the cases studied.

Over 80 per cent of the patients with total cholesterol above 300 mg. per 100 cc. showed an abnormally high readily extractable fraction.

This fraction was roughly normal in most cases in which the total cholesterol was below 300 mg.

The tendency for increased cholesterol extraction, with increased extraction time, is much greater in patients with xanthelasma than in normal persons.

The administration of a pancreatin preparation, high in lipase, to xanthelasma patients with hypercholesteremia seemed to bring about a reduction of the readily extractable fraction in some cases but not in others.

Miss Olga Petterson assisted in the carrying out of most of the laboratory work. Drs. Allen Pepple, Thomas W. Murrell Jr. and DuPont Guerry III referred to us some of the patients involved in this study.

ABSTRACT OF DISCUSSION

DR. ROY L. KILE, Cincinnati: This report by Fowlkes and Forbes represents a great deal of effort—much more than is superficially apparent. The authors have been quite conservative in their conclusions.

We are rapidly becoming aware of the importance of the cholesterol-containing fraction of the lipids in the body. Furthermore, the routine quantitative serum determinations of both cholesterol and total fat are apparently not adequate, and routine examinations of blood serum are not giving us enough information for a proper interpretation. Certain fractions of cholesterol may be offending agents in many diseases. This contention has been made by many authors in recent years. The amount of total cholesterol is not always the important factor. We are undoubtedly on the verge of some major discoveries in this field of blood chemistry.

While the skin disease under consideration is a comparatively minor one (except for its cosmetic aspect) it may be of tremendous importance in calling to our attention changes which are occurring in the cholesterol metabolism in the body generally. As has been pointed out by the authors, these changes may indicate impending atherosclerosis, coronary artery disease and other more serious medical problems. To discover the exact fraction of cholesterol involved is difficult. It may be that Forbes has the solution to the problem.

I think many of us may have been negligent in properly investigating the systemic picture in individuals having xanthelasma.

It may be that the fraction of cholesterol with which the present authors are dealing is the same as the one that Gofman and his group, while working at the University of California, separated off with the ultracentrifuge. Gofman and co-workers very definitely demonstrated the importance of that fraction of cholesterol in atherosclerosis both in the rabbit and in man. Incidentally, it has been repeatedly demonstrated that atherosclerosis can be produced rather regularly in the rabbit by the administration of a high cholesterol diet. Gofman also lowered the amount of S_f 10-20 molecules of cholesterol in blood by restricting cholesterol

ingestion. However, cholesterol may be synthesized in the body, even with acetic acid as the beginning compound, as was brought out by Schoenheimer.

G. H. Becker and his group showed that changes in the fat tolerance of many individuals varied as they grew older. They also found that these changes might be corrected by using a preparation such as polysorbate 80 or a lipase. Their work was with the physical state of the cholesterol rather than the amount present.

The present authors have quite correctly followed through with their work in trying out one of these preparations. Theoretically, lipase should not be effective. As an enzyme it breaks down lipid in the intestinal tract when used orally, as it was. This action might produce more absorption of fats or their derivatives.

While results have not been dramatic, Fowlkes and Forbes may be on the right track. It may be that another chemical, when ingested, will keep down the proper fractions of cholesterol so that they are below a point where depositions of fat occur in the vascular tree. There are many, including Cowdry, who have expressed the opinion that atherosclerosis is more than the deposition of certain types of lipids in the vessels. They have stated that much of it is a secondary process. As a result, this problem is a very complicated one.

The picture of lipid metabolism, which is rapidly assuming the important place that it deserves, is gradually being worked out. It is very fortunate that most of these processes are reversible ones in animals—and, we hope, also in human beings. The possibilities for therapy are quite good.

In the study presented today we have another example of a dermatological problem which, though seemingly trivial, allows dermatologists to point the way to other fields of medicine. I certainly hope that Fowlkes and Forbes will continue this work and that Dr. Fowlkes, who is one of the subjects concerned in the study, may never be involved himself with the disease which he is studying.

DR. HOWARD HAILEY, Atlanta, Ga.: Several years ago a physician's wife consulted me. She had extensive xanthelasma involving the upper and lower lids of both eyes. I sent some of her blood to the Department of Agriculture in Washington for examination with regard to the cholesterol content and received an answer that the normal cholesterol limits were so wide that the examination was of no significance.

I think that Dr. Fowlkes has called to our attention an examination that is going to prove to be very worth while in dermatology, and it may save many of us from early coronary disease. I have had a recent serious illness, and the thing that saved me was the determination of a young physician, so I have been told. I was roaming around in another world, and it was the examination of the calcium content of my blood which gave the clue to the diagnosis. Now I have a greater respect for the study of the chemistry of the blood.

Most of us have come along all these years thinking that the chemical examination of the blood as done in the average laboratory is unimportant.

Dr. Fowlkes's paper has been most stimulating and may prove invaluable in the future management of xanthelasma.

DR. HARRY L. ARNOLD JR., Honolulu, Hawaii: I should like to ask the authors whether they made any comparisons of the level of readily extractable cholesterol with the level of cholesterol esters.

DR. RICHARD W. FOWLKES, Richmond, Va.: I appreciate the discussion very much, and there is little to add. I do feel that Dr. Forbes's tests give valuable information regarding the cholesterol disturbances in the body, and I am personally very much interested in their clinical applications.

In answer to Dr. Arnold's question, Dr. Forbes's studies show that the readily extractable fraction apparently always consists of both free and ester cholesterol.

BISMUTH PENICILLIN IN THE TREATMENT OF ACUTE SYPHILITIC ORCHITIS OF RABBITS

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AND
JOHN A. KOLMER, M.D.
With the Technical Assistance of Anna M. Rule
PHILADELPHIA

THE TREATMENT of syphilis in human beings with penicillin alone usually results in failures averaging from 15 to 20 per cent. Thus L. Altschuler and co-workers [1] reported on a large number of patients so treated an incidence of failure in seronegative primary syphilis of 8.7 per cent, in seropositive primary syphilis of 18.6 per cent and in secondary syphilis of 28.3 per cent. Other observers have reported similar results. It is thus apparent that treatment with penicillin alone is not the complete answer to this problem.

In 1947 Monash [2] prepared a number of insoluble salts of penicillin the administration of which, because of their slow rate of absorption, resulted in the production of prolonged penicillin blood levels in rabbits. One of these salts, namely bismuth penicillin, immediately suggested itself as a possible improvement over penicillin alone in the treatment of syphilis.

Kolmer and Rule during the past few years have been studying the synergistic and additive effects of penicillin and various other spiro-

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The bismuth penicillin was prepared and supplied by Sharp & Dohme, Inc., Philadelphia.

From the Department of Dermatology, New York Medical College, Flower and Fifth Avenue Hospitals, Dr. E. F. Traub, director, and from the Institute of Public Health and Preventive Medicine of Temple University, Dr. John A. Kolmer, director.

1. Altschuler, L.; Karpinos, B. D.; Leifer, W., and Ozog, J. J.: Efficacy of Penicillin Treatment of Early Syphilis in the Army, Am. J. Syph., Gonor. & Ven. Dis. **33**:126, 1949.

2. Monash, S.: Use of Insoluble Penicillin Salts for the Prolongation of Penicillin Blood Levels, Science **106**:370, 1947; Use of Bismuth, Silver and Mercury Salts of Penicillin for the Prolongation of Penicillin Blood Levels, J. Invest. Dermat. **9**:157, 1947.

cheticidal agents, such as oxophenarsine hydrochloride,[3] bismuth salicylate,[3] bismuth potassium tartrate,[4] sodium iodide [5] and tryparsamide.[6] They have found each of the above-mentioned substances to have either a synergistic or an additive effect with penicillin in the treatment of rabbit syphilis. Magnuson and co-workers [7] confirmed Kolmer and Rule's observations with bismuth and penicillin, also reporting that the most efficient results in the treatment of rabbit syphilis were obtained when the bismuth and penicillin were given together from the very beginning of the treatment.

It was therefore thought advisable to study the curative action of bismuth penicillin in acute rabbit syphilitic orchitis, since this compound would supply in one injection a combination of two synergistic or additive spirocheticidal substances.

TECHNIC EMPLOYED

The bismuth penicillin used was a suspension in sesame oil, with 2 per cent aluminum monostearate, containing 200,000 units of penicillin per cubic centimeter. Commercial sodium penicillin G suspended in peanut oil and white wax was used as a control compound. Dilutions of each compound were made with sterile peanut oil.

Both compounds were administered by intramuscular injection in two treatment schedules, namely (*a*) single doses and (*b*) one dose per day for eight days in succession. Each dose was given in terms of units per kilogram of body weight.

Rabbits weighing from 1,800 to 2,200 Gm. were inoculated intratesticularly with the Nichols-Hough strain of Treponema pallidum. Treatment was instituted about six weeks later in rabbits acquiring acute syphilitic orchitis with strongly positive results on dark field examinations (rated as 4 in tables). Dark field examinations were made 1, 2, 3, 7, 14, 21, 28, 35, 42, 56 and 70 days after the first doses.

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3. Kolmer, J. A.: Synergistic or Additive Activity of Penicillin by Oral Administration with Oxophenarsine Hydrochloride ("Mapharsen") by Intravenous and Intramuscular Injection and Bismuth Salicylate by Intramuscular Injection, Arch. Dermat. & Syph. **57**:965 (June) 1948.

4. Kolmer, J. A.: Synergistic or Additive Activity of Penicillin, Oxophenarsine Hydrochloride and Bismuth and Potassium Tartrate, Arch. Dermat. & Syph. **56**:179 (Aug.) 1947.

5. Kolmer, J. A.: Penicillin in the Treatment of Experimental Syphilis of Rabbits: Synergistic or Additive Activity of Penicillin Injected Intramuscularly with Sodium Iodide Administered Orally and Intravenously, Arch. Dermat. & Syph. **61**:49 (Jan.) 1950.

6. Kolmer, J. A.: Penicillin in the Treatment of Experimental Syphilis of Rabbits: Synergistic or Additive Activity of Penicillin Injected Intramuscularly and Tryparsamide Administered Intravenously, Arch. Dermat. & Syph. **61**:56 (Jan.) 1950.

7. Magnuson, H. J., and Rosenau, B. J.: Bismuth Plus Penicillin in Treatment of Experimental Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **32**:203, 1948.

Lymph node transfers were made to fresh rabbits four weeks after the last doses. These rabbits were kept under observation for about 4 months, after which the results were evaluated.

TABLE 1.—*Results of Administration of Bismuth Penicillin in Sesame Oil and 2 per Cent Aluminum Monostearate, 200,000 Units per Cubic Centimeter, in Single Doses of Intramuscular Injection*

Rabbit No.	Dose, Units per Kg.	Results of Dark Field Examination for T. Pallidum, Days*											Results of Lymph Node Transfers
		1	2	3	7	14	21	28	35	42	56	70	
1	100,000	2	1	—	—	—	—	—	—	—	—	—	—
2	100,000	2	1	—	—	—	—	—	—	—	—	—	—
3	50,000	3	2	2	—	—	—	—	—	—	—	—	—
4	50,000	3	2	1	—	—	—	—	—	—	—	—	—
5	25,000	4	2	2	—	—	—	—	—	—	—	—	—
6	25,000	4	1	1	—	—	—	—	—	—	—	—	—
7	10,000	4	2	1	—	—	—	—	—	—	—	—	—
8	10,000	4	1	—	—	—	—	—	—	—	—	—	—
9	5,000	4	2	—	—	—	—	—	—	—	—	—	—
10	5,000	4	3	1	—	—	—	—	—	—	—	—	+

*After institution of treatment: 4 indicates large numbers of actively motile treponemes; 3, 2 and 1 indicate smaller numbers of treponemes per dark field, respectively; — indicates negative results.

TABLE 2.—*Results of Administration of Sodium Penicillin G in Peanut Oil and White Wax, 300,000 Units per Cubic Centimeter, in Single Doses by Intramuscular Injection*

Rabbit No.	Dose, Units per Kg.	Results of Dark Field Examination for T. Pallidum, Days*											Results of Lymph Node Transfers
		1	2	3	7	14	21	28	35	42	56	70	
1	100,000	2	1	—	—	—	—	—	—	—	—	—	—
2	100,000	2	1	—	—	—	—	—	—	—	—	—	—
3	50,000	3	1	—	—	—	—	—	—	—	—	—	—
4	50,000	3	2	1	—	—	—	—	—	—	—	—	—
5	25,000	4	2	1	—	—	—	—	—	—	—	—	—
6	25,000	4	2	2	—	—	—	—	—	—	—	—	—
7	10,000	4	2	1	—	—	—	—	—	—	—	—	+
8	10,000	2	1	1	—	—	—	—	—	—	—	—	—
9	5,000	4	2	2	—	—	—	—	—	—	—	—	+
10	5,000	3	2	2	—	—	—	—	—	—	—	—	+

*After institution of treatment: 4 indicates large numbers of actively motile treponemes; 3, 2 and 1 indicate smaller numbers of treponemes per dark field, respectively; — indicates negative results.

RESULTS

The minimal single curative dose of bismuth penicillin was found to be approximately 5,000 units per kilogram of weight (table 1), and the minimal single curative dose of sodium penicillin G in peanut oil and white wax was approximately 10,000 units per kilogram of weight (table 2).

The minimal total curative dose of bismuth penicillin administered once a day for eight days in succession was approximately 4,000 units per kilogram of weight, approximately 500 units per dose (table 3), and

the minimal total curative dose of sodium penicillin G in peanut oil and white wax administered once a day for eight days in succession was approximately 8,000 units per kilogram of weight, approximately 1,000 units per dose (table 4).

TABLE 3.—*Results of Administration of Bismuth Penicillin in Sesame Oil and 2 per Cent Aluminum Monostearate, 200,000 Units per Cubic Centimeter, Once a Day for Eight Days in Succession by Intramuscular Injection*

Rabbit No.	Dose, Units per Kg.	Total Dose, Units per Kg.	Results of Dark Field Examinations for T. Pallidum, Days*											Results of Lymph Node Transfers
			1	2	3	7	14	21	28	35	42	56	70	
1.....	2,000	16,000	3	2	1	—	—	—	—	—	—	—	—	—
2.....	2,000	16,000	4	2	1	—	—	—	—	—	—	—	—	—
3.....	1,000	8,000	4	3	1	—	—	—	—	—	—	—	—	—
4.....	1,000	8,000	4	2	1	—	—	—	—	—	—	—	—	—
5.....	500	4,000	4	4	3	—	—	—	—	—	—	—	—	—
6.....	500	4,000	4	4	2	—	—	—	—	—	2	3	3	+
7.....	250	2,000	4	4	3	—	—	—	—	—	—	—	—	+
8.....	250	2,000	4	3	1	—	—	—	—	—	—	—	—	+
9.....	100	800	4	4	4	—	—	—	3	4	4	4	4	+
10.....	100	800	4	4	4	—	—	2	4	4	4	4	4	+

* After institution of treatment: 4 indicates large numbers of actively motile treponemes; 3, 2 and 1 indicate smaller numbers of treponemes per dark field, respectively; — indicates negative results.

TABLE 4.—*Results of Administration of Sodium Penicillin G in Peanut Oil and White Wax, 300,000 Units per Cubic Centimeter, Once a Day for Eight Days in Succession by Intramuscular Injection*

Rabbit No.	Dose, Units per Kg.	Total Dose, Units per Kg.	Results of Dark Field Examinations for T. Pallidum, Days*											Results of Lymph Node Transfers
			1	2	3	7	14	21	28	35	42	56	70	
1.....	3,000	24,000	2	1	1	—	—	—	—	—	—	—	—	—
2.....	3,000	24,000	3	1	—	—	—	—	—	—	—	—	—	—
3.....	2,000	16 000	2	1	1	—	—	—	—	—	—	—	—	—
4.....	2,000	16,000	2	1	—	—	—	—	—	—	—	—	—	—
5.....	1,000	8,000	3	2	1	—	—	—	—	—	2	3	3	+
6.....	1,000	8,000	2	1	1	—	—	—	—	—	—	—	—	—
7.....	500	4,000	3	2	2	—	—	—	—	—	—	—	—	+
8.....	500	4,000	3	1	1	—	—	—	—	—	—	—	—	+
9.....	250	2,000	4	2	2	—	—	—	—	—	—	—	—	+
10.....	250	2,000	4	1	1	—	—	—	—	—	—	—	—	+

* After institution of treatment: 4 indicates large numbers of actively motile treponemes; 3, 2 and 1 indicate smaller numbers of treponemes per dark field, respectively; — indicates negative results.

Bismuth penicillin is a whitish crystalline substance containing three molecules of penicillin combined with one atom of trivalent bismuth. Its correct technical name is therefore either bismuth tripenicillinate or bismuth tripenicillate. For the sake of convenience we will continue to use the term bismuth penicillin. Its molecular weight is approximately 1,209 with a theoretical bismuth content of 17.29 per cent. The bismuth penicillin used in this investigation contained 17.05 per cent of bismuth.

The suspension in 2 per cent aluminum monostearate gelled in sesame oil contained 0.255 mg. of bismuth per 1,000 units of penicillin or 1.279 mg. per 5,000 units. For clinical trials in the treatment of syphilis it is suggested that doses of 400,000 to 600,000 units per injection be used, containing approximately 0.1 to 0.15 Gm. of bismuth.

SUMMARY

Bismuth penicillin suspended in sesame oil with 2 per cent aluminum monostearate is approximately twice as curative as sodium penicillin G suspended in peanut oil and white wax in the treatment of acute syphilitic orchitis in rabbits.

1475 Broadway, New York 18 (Dr. Monash).

2101 Pine Street, Philadelphia 3 (Dr. Kolmer).

Clinical Notes

NOTE ON THE EXPERIMENTAL USE OF RABIES VACCINE FOR MELANOMATOSIS

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In May 1940 a 32 year old woman with a malignant melanoma 3 cm. in diameter and situated in the pretibial region had the lesion surgically excised on the mixed tumor service of the Memorial Hospital. An elective groin dissection six weeks later revealed no deposits of metastatic melanoma in regional nodes. In September 1942 three cutaneous melanotic nodules were excised from the same leg and thigh. In September 1943, after a dog bite, the patient received 14 injections of rabies vaccine. In April 1948 two additional melanotic nodules were removed from the skin on the ipsolateral side. At this writing, two years later, there had been no further evidence of recurrence.

The long latent period of 5½ years intervening between the appearance of multiple metastases was so extraordinarily unusual that it excited considerable speculation among various members of the clinic staff concerning the cause of this inhibition. In a personal experience totaling more than 1,000 cases of malignant melanoma, we had occasionally noted local recurrence or distant metastasis five or more years after removal of the primary lesion, but not such a long interval between the appearances of multiple cutaneous metastases.

The only incident in the patient's case history which might be of related interest was the program of immunization against rabies. Virus inoculation in experimental attempts at control or cure of tumors in animals has yielded variable but occasionally promising results, but often with disappointing sequelae. On the empiric basis of this related coincidence it was decided to give similar series of rabies vaccine to some patients with generalized melanomatosis. This clinical experiment is still continuing in the Laboratory for Clinical Investigation at the Memorial Hospital. I have administered the vaccine to a group of 12 private patients, chosen because of the prospect of better control and with their knowledge of the procedure.

Consecutive daily intramuscular inoculations of the Harris rabies vaccine were given for 20 days, and in some instances the total dose was repeated. In 10 patients no apparent changes in the existing tumors were observed and the inevitable course of the disease was apparently uninfluenced. In one patient with innumerable black, elevated nodular cutaneous metastases involving the face, neck, breasts, trunk, abdomen and thighs the nodules became macular and flat with loss of all induration but persistence of pigmentation. With eyes closed the examiner could no longer palpate the nodules in the skin, and no new lesions were apparent in the course of the next four months. Three of the macular pigmented spots were excised for microscopic study; with disappointment but without surprise, residual fully active melanoma cells were seen in each specimen.

Another patient had an enucleation of an eye for melanoma in 1936. Abdominal exploration at the time of a laparotomy for uterine myomectomy in 1949 revealed a spherical black tumor in the right hepatic lobe. This known metastasis in the liver grew with great rapidity, and in a few months the large firm liver occupied almost the entire right side of the abdomen and extended well below the anterior part of the superior iliac spine. Two series of rabies vaccine, each of 20 daily

doses, were given within a three month interval. The regression in size was dramatic as the liver edge receded to the costal margin, but the nodule, now quite small, could still be palpated. The patient's health improved, and at the end of six months she weighed more than at any previous time in her life. A laparotomy was then performed, and the single multilobular melanotic metastasis was surgically excised from the right lobe of the liver. The tumor was viable, and there were no cellular alterations seen on microscopic study. The future duration of palliation, of course, cannot be predicted.

I am motivated in publishing this incomplete and unsuccessful story at this premature time by the unfortunate fact that news of this experiment has become widely disseminated. I have been besieged by innumerable telegrams, letters and telephone calls begging for more specific information. In self protection and with the wish of stopping the hope this false rumor has inspired, I have reported the experience of my associates and myself to date.

DERMATITIS FROM ORANGE I IN A CANDY FACTORY

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LANCASTER, PA.

This outbreak of dermatitis is reported because of its intrinsic interest and the possibility of an unrecognized health hazard for the general public, especially children.

Workers in a candy factory began to complain of an "itching rash" on their hands and occasionally on the neck and face. Their plant was working to capacity preparing for the Halloween business rush, for which their products had wide distribution. Because of rapid labor turnover, it is difficult to determine how many workers had been exposed and their subsequent histories, but at least four girls out of approximately 100 in the department concerned complained and were examined.

The workers principally involved were "baggers." Their duty was to squeeze marshmallow from large cloth bags and then manually form stars, pumpkins, etc. The resultant shapes were then covered with various tinted sugars and dried, packed and sold—without further processing. The workers themselves blamed the marshmallow and an orange-tinted sugar for their troubles.

Patch tests with white granulated sugar, four colored sugars, marshmallow and its individual components gave negative reactions except those with the orange-tinted sugar, to which reactions were strongly positive.

One test subject complained of sufficient itching to demand immediate removal of the patch. Her arm near the patch site had rapidly become erythematous. Another subject manifested a bulla after wearing the patch for 48 hours.

The custom in this plant was to add various dyes to plain granulated sugar in order to obtain the proper tint for the desired decorations. The orange dye was used to obtain the rich orange color for Halloween candies. It seemed unlikely that the marshmallow was causing the trouble until it was learned that the bags containing the marshmallow occasionally became covered with the orange sugar, this in turn contacting the workers' hands.

The dye giving the Halloween orange has the name of orange I and is chemically the sodium salt of *p*-sulfobenzene azo-alpha-naphthol. It was one of the first aniline dyes to be synthesized and has been well known as causing sensitization.

After this substance was removed from the work tables and candy, no further cases of dermatitis occurred although all procedures continued exactly as before except that other dyes were used. The dermatitis of those affected quickly subsided under symptomatic treatment and had not recurred to the time of writing. The factory management stated that they had received no complaints of dermatitis or gastrointestinal disorders from consumers of their Halloween candies.

230 North Duke Street.

HETEROTOPIC BONE IN A PIGMENTED NEVUS

LEONARD MELTZER, M.D.
HOUSTON, TEXAS

Osteoma cutis, either primary or secondary, occurs very rarely, as is evidenced by the fact that Hopkins [1] in reviewing the literature in 1928 could find only five cases. During the next 20 years Leider [2] could uncover only seven additional cases. Such calcifications have reportedly occurred in ulcers, cysts, scars, lupus erythematosus, acne vulgaris and scleroderma and finally as embryonic cell rests. The only case previously recorded in which true bone was found in a pigmented nevus was that of Heidingsfeld.[3] The case herein described bears some resemblance to that one.

REPORT OF A CASE

A 42 year old white woman was referred for treatment of a pigmented lesion on the right cheek which had been present since childhood. This had increased considerably in size during the preceding months and had become slightly tender.

One inch (2.5 cm.) above and lateral to the right angle of the mouth there was a dark brown tumor, 0.5 cm. in diameter. A few hairs protruded above the surface. Moderate pressure on the lesion caused some tenderness. There was no surrounding inflammation, and no regional adenopathy was evident. Because of the story of recent enlargement and tenderness it was felt that excision was the proper treatment. This was performed with the use of local anesthesia.

The pathologic report as rendered by Dr. Fred Weidman was as follows: "The epidermis was thin. At one end of the section only minor infiltration of lymphocytes appeared around the blood vessels. However, the significant lesion in the case was an intradermal nevus which occupied practically all the remaining portion of the section. The nevus cells extended almost from the epidermis and fell barely short of the bottom of the section. These were arranged in the classic groups and alveoli. At the bottom of the section a region of inflammatory tissue appeared. It was sharply outlined and consisted of a reticulum on which numerous lymphocytes and foreign body giant cells were disposed.

At another place, near the bottom of the section, two collections of osseous tissue appeared. They were rounded and unassociated with any significant inflammatory reaction. One of them was definitely calcified, and the other only slightly, and fatty marrow occupied the center of one."

Dr. Weidman's conclusions and summary, which stimulated my investigation, stated that "This heterotopic bone is rare in these nevi but is by no means unknown.

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1. Hopkins, J. G.: Multiple Miliary Osteomas of the Skin: Report of Case, Arch. Dermat. & Syph. **18**:706 (Nov.) 1928.
2. Leider, M.: Osteoma Cutis, Arch. Dermat. & Syph. **58**:169 (Aug.) 1948.
3. Heidingsfeld, L. M.: Osteoma Cutis, Arch. f. Dermat. u. Syph. **92**:337, 1908.

The inflammatory focus, with its giant cells, was probably the result of preexisting inflammation of hair follicles which had largely cleared up. As a matter of fact, I have observed actually suppurative lesions in these nevi, which have caused a rather sudden enlargement of the lesion which has been mistaken for rapid growth of the nevus."

COMMENT

The sudden enlargement of this apparently benign nevus can be explained pathologically by the region of lymphocytes around the blood vessels. Some inflammation of the hair follicles which in its subsiding stage left this focus of lymphocytes had probably occurred. The occurrence of bone tissue with no surrounding cellular infiltration would seem to rule out any degenerative process. Lack of connection with glands, hair or any type of necrosis would seem to rule out metaplasia. The explanation would seem to be that the bony element represented embryonic cell rests.

SUMMARY

A case of heterotopic bone in a simple pigmented nevus is reported. This is the second case to appear in the literature in over 40 years. The pathologist's report would seem to support the theory of the origin of the bony tissue that it arose from embryonic cell rests.

BCG VACCINATION IN SARCOIDOSIS

Preliminary Report

THEODORE CORNBLEET, M.D.
CHICAGO

Sarcoidosis may involve the skin primarily with a variety of lesions and in addition affect other tissues and systems. Thus, the lymph glands, bones and various viscera may be involved. The debate about the etiology of this disease has been warm and extensive, with the clearest overtones heard with regard to a tuberculous cause.

The majority of subjects react negatively to tuberculin even in high concentration, and most of the minority show weakly positive reactions. It has been held that a special immunologic state in sarcoidosis decreases or entirely prevents the positive reaction to tuberculin which otherwise would be present to indicate the underlying tuberculous infection.

When persons with negative reactions to tuberculin, who presumably, therefore, are free from past or present tuberculous infection, are inoculated with BCG vaccine, 90 per cent manifest positive reactions in two weeks and about 100 per cent do so in four weeks.[1] It was interesting, therefore, to see whether the nonreactors to tuberculin who had sarcoidosis would change their response to this antigen after being vaccinated. It was felt that the results would have some bearing in the discussion over the etiology of sarcoidosis, for if BCG produced a positive tuberculin reaction that occurrence would weaken the argument for a tuberculous infection as the cause of sarcoidosis. On the other hand, if the response to tuberculin still remained negative in the face of BCG vaccination, then that result would strengthen the argument in favor of a tuberculous etiology of sarcoidosis. One wonders what responses would occur to other antigens.

From the Departments of Dermatology, University of Illinois College of Medicine and the Cook County Hospital.

1. Results in 600 adults studied at the Tice Laboratories and Institution for Tuberculous Research, Chicago.

Six patients with sarcoidosis verified by biopsies of the skin and lymph glands were inoculated with BCG vaccine by the multiple puncture method developed by Rosenthal.[2] Five of these gave negative reactions to tuberculin, and the sixth, a positive one to 1 to 100 material. The vaccination was successful in all cases, as indicated by the characteristic papules preesnt at the site of inoculation. One subject continued to give negative reactions to tuberculin for six months after the inoculation and then showed a positive reaction. The patient who gave positive reactions to tuberculin before the inoculation continued to give positive ones afterward with no change in the intensity of response. The other four have continued to give negative reactions to tuberculin for three to six months, the period during which they had been observed to the time of writing.

The course of sarcoidosis is unpredictable, with spontaneous improvement and apparent cure occurring frequently. It is, therefore, not to be emphasized though noteworthy that in four[3] of the group mentioned above there was early improvement or complete resolution of the cutaneous lesions and sarcoidal changes elsewhere. Though the number is small in whom this result took place, the occurrence would seem to encourage the trial of BCG vaccine as a therapeutic agent and for further observations in sarcoidosis. The full report of these cases will be published later.

Dr. S. R. Rosenthal especially and Drs. S. Barsky, D. Musgrave and D. L. Fuhrman assisted me in this study.

2. Rosenthal, S. R.: The Multiple Puncture Method of BCG Vaccination, Am. Rev. Tuberc. **39**:128, 1939; Vaccination by Means of the Powdered Antigen (Freeze-Dried) and the Multiple Puncture Disc, Ann. Inst. Pasteur **75**:497 (Dec.) 1948.

3. Only these four were observed for therapeutic response; the other two patients reported on in this paper were seen by Dr. S. R. Rosenthal alone.

AMYLOIDOSIS CUTIS, LICHENOID TYPE, TREATED SUCCESSFULLY WITH RESIN OF PODOPHYLLUM

JOHN GARB, M.D.
NEW YORK

The following case of amyloidosis cutis is herewith reported because of the rapid regression of the lesions, with almost complete relief from itching in two weeks, following applications of resin of podophyllum ointment.

REPORT OF A CASE

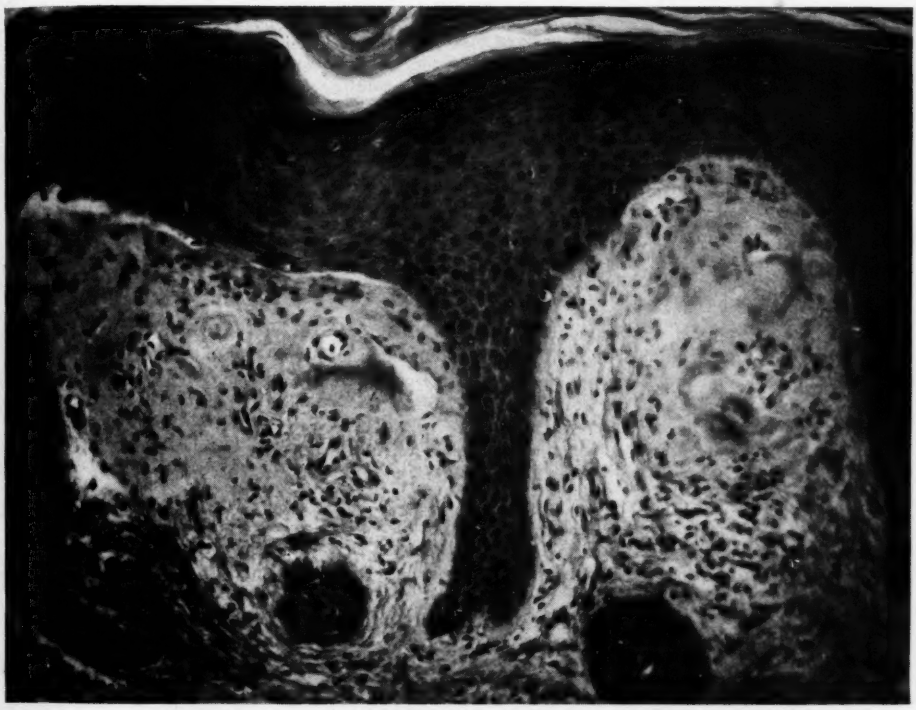
History.—U. S. E.,[1] a man aged 79, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 7, 1944,

From the New York Skin and Cancer Unit, Department of Dermatology and Syphilology, Dr. Marion B. Sulzberger, director, Post-Graduate Medical School, New York University–Bellevue Medical Center.

1. The patient was presented before the New York Dermatological Society on Dec. 19, 1944, by Dr. Fred Wise; before the Manhattan Dermatologic Society on Jan. 9, 1945, by Dr. Max Scheer as having "Amyloidosis Cutis," and before the Bronx Dermatological Society on April 15, 1948, by Dr. John Garb as having "Amyloidosis Cutis Treated with Resin of Podophyllum."

presenting lesions of about fifteen years' duration. There was no history of a similar disease in the family. He had worked as a post office clerk for forty-five years. He had contracted pneumonia in 1929 but had been in good health since.

The eruption had begun on the back of the right ankle in 1929 and then spread to the outer surface on the right foot. It extended gradually and continuously, enlarging in five years to about 10 cm. Similar lesions appeared in 1938 on the left calf. In about a year the eruption "disappeared" from the left leg but recurred in 1943. The patient had no pain but complained that the lesions itched.



Photomicrograph of the biopsy specimen taken from the lesion of the right leg, showing areas of darker staining homogeneous amyloid masses in the papillary zones; × 160.7.

Dermatologic Examination.—Commencing at the ankle and extending to the junction of the middle and upper third of the outer and anterior surfaces of the right leg was an eruption which consisted of match-head-sized to split-pea-sized macules and maculopapules, discrete and grouped, forming irregular patches. There were a few similar and somewhat excoriated lesions which were less distinct on the left calf. The patches were raised, yellowish red and rather shiny. Some were smooth, but others were slightly rough to the touch and covered with very fine adherent scaling. They were hard, painless, nontender, infiltrated and nonelastic. They did not change on diascopic pressure. The rest of the cutaneous surface appeared

normal. There were no lesions in the oral mucosa. The pupils reacted well to light and in accommodation. The results of routine laboratory tests were normal.

Histologic Observations.—A histologic section of one of the nodules stained with hematoxylin and eosin was interpreted by Dr. Charles F. Sims as follows: "The epidermis was moderately and irregularly acanthotic. It was covered by a fairly compact but moderately hyperkeratotic layer. In the papillary and subpapillary zones the collagen stained rather faintly. The capillaries in the papillary bodies were moderately dilated (figure). The slide stained with methylrosaniline chloride revealed a positive reaction for amyloid."

Treatment and Course.—One patch was treated with three applications of solid carbon dioxide once weekly without apparent benefit. From Jan. 13 until Nov. 20, 1947, the patient was treated with superficial roentgen ray exposures. A total of 750 r (10 times 75 r) was given to the right leg and 150 r (2 times 75 r) to the left leg. There was no perceptible improvement.

On Jan. 9, 1948, a 2.5 per cent resin of podophyllum ointment was applied to the patches of the right leg with a cotton applicator. The base consisted of 10 parts of castor oil and 45 parts each of aquaphor® (an oxycholesterol-petrolatum ointment base) and white petrolatum. A dressing of wax paper and gauze was bandaged on for twenty-four hours. The leg became somewhat inflamed but the inflammation was relieved by the use of a soothing ointment consisting of bismuth subgallate, 4.0 Gm.; castor oil, 6.0 Gm.; aquaphor,® 8.0 Gm., and white petrolatum, sufficient to make 30.0 Gm.

The normal skin for an area of 1 inch (2.5 cm.) beyond the edges of the lesions was coated with flexible collodion, which procedure has been found to be a satisfactory way of protecting the unaffected skin from the resin of podophyllum. A resin of podophyllum ointment of 0.5 per cent strength was applied by the patient every day for ten days and several times subsequently. Between June 21 and Sept. 25, 1948, the resin of podophyllum was reapplied six times about once every three weeks, 2.5 per cent being used for the first four and 5.0 per cent for the last two applications.

Examination on March 11, 1949, showed that the legs were smooth, presenting only a few slightly raised macules and numerous brownish-pigmented match-head-sized to split-pea-sized spots at the sites of the former lesions. The patient stated that he was completely free from itching.

There was no evidence of systemic reaction due to absorption of resin of podophyllum, which if it had occurred would probably have been manifested mainly by gastrointestinal symptoms.

COMMENT

The patient had unequivocal amyloidosis cutis, the clinical diagnosis having been confirmed histologically by the characteristic violet-red staining of the amyloid deposits with methylrosaniline chloride, as Nomland [2] stated that "red staining of deposits of amyloid with methyl violet is the most diagnostic reaction of amyloid." The patient refused testing with intracutaneous injections of congo red as developed by Nomland.[3] The diagnosis of amyloidosis cutis was also accepted without reservations at the meetings of the dermatologic societies where the patient was presented.[1]

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2. Nomland, R.: Localized (Lichen) Amyloidosis of the Skin, Arch. Dermat. & Syph. **33**:95 (Jan.) 1936.

3. Nomland,[2] p. 96.

Interest in resin of podophyllum was stimulated by the report of Kaplan [4] of its successful use in condylomata acuminata. I have used this drug with good results in neurodermatitis [5] and in some cases of lichen chronicus simplex and psoriasis. A report on these cases will be made in the near future.

The pharmacology of resin of podophyllum was covered recently by Sullivan,[6] and comments on the subject will not be repeated here.

Mode of Action.—Resin of podophyllum does not seem to exert its effect as an escharotic such as a strong acid or caustic alkali, which destroys dead and living tissue, especially proteins. It appears, when used in its proper concentration, to act more like a digestant of the diseased tissue. Sullivan and King [7] made histologic studies on condylomata acuminata and verrucae vulgares treated with resin of podophyllum. They stated that "It appears that resin of podophyllum exerts a profound and subtle action on cell metabolism, in contrast to salicylic or trichloroacetic acid which produces a simple 'fixing' or coagulation effect." They expressed the belief that the main effect of resin of podophyllum appears to be directly on the epithelial cells, one action being of a direct degenerative character, and another, "the production of bizarre cell forms interpreted as distorted mitotic figures . . . called 'podophyllin cells,' . . . similar to so-called colchicine figures."

Sullivan and King [8] stated the opinion that podophyllotoxin may be the component in resin of podophyllum responsible for its cytotoxic effect. They found that application of 20 per cent of resin of podophyllum in 95 per cent alcohol caused rapid regression of lesions in all the 29 patients with condylomata acuminata, while resin of podophyllum dissolved in a solution of potassium and sodium hydroxide was inert. This inert action may rightly be attributed to the fact that podophyllotoxin is easily hydrolyzed in these alkaline solutions [9] and changed by rearrangement to its inert isomer picropodophyllin.[10] However, Ormsbee [11] and his associates showed that podophyllotoxin is not as effective as resin of podophyllum in causing selective damage on mouse tumor cells in tissue culture.

Discussion of Treatment.—Wax paper was used and the area bandaged for one day so that the amyloid patches would be in continuous contact with the resin of podophyllum ointment using a base consisting of castor oil, aquaphor® and petro-

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4. Kaplan, I. W.: Condylomata Acuminata, New Orleans M. & S. J. **94**:338, 1942.

5. Garb, J.: Neurodermatitis Treated with Resin of Podophyllum, Arch. Dermat. & Syph. **61**:690 (April) 1950.

6. Sullivan, M.: Podophyllotoxin, Arch. Dermat & Syph. **60**:3 (July) 1949.

7. Sullivan, M., and King, L. S.: Effect of Resin of Podophyllum on Normal Skin, Condylomata Acuminata and Verruca Vulgaris, Arch. Dermat. & Syph. **56**:45 (July) 1947.

8. Sullivan and King,[7] pp. 38 and 45.

9. Viehover, A., and Mack, H.: Biochemistry of May Apple Root (Podophyllum Peltatum), J. Am. Pharm. A. **27**:632, 1938.

10. Jenkins, G. L., and Hartung, W. H.: The Chemistry of Organic Medical Products, ed. 2, New York, John Wiley & Sons, 1947, p. 278.

11. Ormsbee, R. A.; Cornman, I., and Berger, R. E.: Effect of Podophyllin on Tumor Cells in Tissue Culture, Proc. Soc. Exper. Biol. & Med. **66**:590, 1947.

latum. The effectiveness of the treatment is attributed to the employment of this vehicle and mode of application in preference to the use of mineral oil, alcohol or compound tincture of benzoin. While for this patient a strength of 2.5 per cent was found to be very effective, and later even 0.5 pe rcent, other patients may require strengths up to 10, 15 and 25 per cent, especially with the nodular type of amyloidosis cutis.

It is my opinion that resin of podophyllum, with its specific effects in condylomata acuminata, granuloma inguinale [12] and some other resistant dermatoses, is one of the most useful additions to the armamentarium in dermatology.

SUMMARY

A case is herewith reported of the healing of patches of the lichenoid type of amyloidosis cutis of twenty years' duration with applications of resin of podophyllum salve after the lesions had failed to respond to an adequate course of roentgen ray exposures.

Resin of podophyllum, 2.5 per cent, incorporated in a special ointment base was applied to the lesions, after which the area was covered with wax paper and gauze and bandaged for twenty-four hours. The patient then used 0.5 per cent salve for ten days. There was pronounced regression of the lesions after two weeks, with complete elimination of itching. Resin of podophyllum salve, 2.5 to 5 per cent, was applied subsequently six times, about once every three weeks, until the lesions completely regressed. There had been no recurrence when the patient was last seen, on April 21, 1949.

219 East Nineteenth Street (3).

12. Tomskey, G. C.; Vickery, G. W., and Gatzoff, P. L.: The Successful Treatment of Granuloma Inguinale with Special Reference to the Use of Podophyllin, J. Urol. **48**:401, 1942.

CASE OF POSSIBLE PREVENTION OF PERMANENT ALOPECIA FOLLOWING ROENTGEN THERAPY

HARRY M. ROBINSON SR., M.D.
BALTIMORE

In our experience as well as that of Lewis and associates [1] roentgen irradiation for the epilation of scalp hair has been found to be the most effective adjunct method in the treatment of tinea capitis.

Occasionally, however, untoward reactions may occur even with as little as 350 to 400 r, principally in the form of itching and few to numerous small pustules.

When a larger dose is administered, dermatitis usually results. MacKee and associates [2] stated that permanent damage to the scalp may result if more than twice the epilating dose is given.

From the Department of Dermatology, University of Maryland School of Medicine.

1. Lewis, G. M.; Hopper, M. E., and Reiss, F.: Ringworm of the Scalp: Clinical Data on Recent Cases; Experiences with Local Endocrine Therapy. J. A. M. A. **132**:62-65 (Sept. 14) 1946.

2. MacKee, G. M.; Mutscheller, A., and Cipollaro, A. C.: Treatment of Tinea Capitis with Roentgen Rays, Arch. Dermat. & Syph. **53**:458-470 (May) 1946.

The prevention of such a serious sequela in a patient to whom a technician gave 800 r to each of four areas seemed worth reporting. The patient was a white girl aged 6 who had received more than double the usual epilating dose, 6 milliamperes having been used instead of 3 and all other factors having been kept the same.

As soon as this error was brought to my attention, the parents were asked to bring the child to me. Erythema was present, and itching was severe.

Ice caps were ordered to be applied to the scalp day and night. The ice cap was covered with double thickness huck towels and was removed frequently or if the patient complained of its hurting. Itching was almost immediately controlled. After three weeks of constant applications of the ice, the parents were permitted provisionally to discontinue this procedure unless itching recurred.

Several attacks of itching did occur in this period and were controlled by the application of ice, but gradually the itching lessened in severity. Eventually the ice caps could be left off, but the patient was completely bald, without the slightest sign of hair or down, and remained so for four months. At this time, the Wood light examination was negative for infection and there were numerous short, soft dark hairs all over the surface of the scalp. Seven weeks later the patient's mother telephoned me, stating that the hair was returning satisfactorily and that examination with the Wood light by the school physician showed no areas of ringworm involvement. The patient is now completely well and has a satisfactory growth of hair.

During the ice application period, the parents were warned that under no condition could this treatment be neglected, as otherwise permanent baldness might result.

COMMENT AND CONCLUSION

A case is presented in which a patient received more than 800 r to each of four areas of the scalp. It is believed that, by prevention of the acute inflammatory reaction that usually follows such a dose by means of the continuous application of ice, exudation, infection and scarring were avoided.

AUTOSENSITIZATION IN INFECTIOUS ECZEMATOID DERMATITIS

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LEXINGTON, KY.
AND
JOSEPH TAMURA, Ph.D.
CINCINNATI

Thirty cases of infectious eczematoid dermatitis were studied and form the basis of this report; 10 of the patients were in preadolescence, and 20 were beyond that stage of life. Involvement of practically every part of the skin was seen in the series, but the ears, nares and face were the predominant sites primarily involved in children, while the legs and feet were the commonest sites of primary involvement in older patients.

The eruption was widespread with id formation in 19 cases (in nine of these cases there was a familial history of allergy) and localized in 11 cases (in only two of these cases was there a familial history of allergy.) Sixteen patients had

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had previous bouts of similar skin disease. All but three of the 30 patients had received local and/or systemic therapy for their current episode prior to seeking the aid of a dermatologist, often with resulting irritation of the existing condition.

As to type of skin, 17 patients had an ichthyotic skin and two had seborrheic skin, while 11 had skin considered to be neither excessively dry nor excessively oily.

Functional instability, endocrine factors and vitamin deficiency were not interpreted as being significant factors. Occupation played a role in instances in which the process was initiated by a contact dermatitis. Cultures of exudate and vesicular fluid were taken with sterile swabs moistened with a sterile isotonic solution of sodium chloride and inoculated onto blood agar plates and into infusion broth. Hemolytic and nonhemolytic types of Staphylococcus aureus and a beta hemolytic streptococcus were cultured most often and with greater numbers of colonies than any other organisms produced.

Inoculation of exudate from the lesion into normal and abraded skin of the upper part of the back was done in 22 cases; the sites were covered with elastopatch® and reexamined in 24 and 48 hours. Mechanical abrasion was done by stroking the site 10 times at light pressure with a Bard-Parker blade, using a lateral rather than a cutting motion. The only reaction obtained was faint erythema along the lines of abrasion.

Number of Times Each Organism Was Isolated

Hemolytic Staph. aureus	14	Aspergillus niger	1
Nonhemolytic Staph. aureus	10	Streptococcus viridans	4
Beta hemolytic streptococcus	8	Corynebacterium diphtheriae	1
Nonhemolytic streptococcus	3	Bacillus subtilus	1
Diphtheroids	3		

Intradermal tests with 0.1 cc. of penicillin G solution (500 units per cubic centimeter) and 0.1 cc. of trichophytin (1:100 dilution) were done in 28 of the cases; at 48 hours there were nine positive reactions to the trichophytin, and none to the penicillin. The patient from whose ear A. niger was cultured had a violent reaction to trichophytin, a 5 cm. area of purpura and edema.

Significantly, 11 of the 30 patients had a familial history of allergy. Nine of these 11 patients had a widespread id eruption when examined.

Therapeutically, wet dressings applied locally, sulfonamides given enterally, penicillin administered intramuscularly and the administration of fractional roentgen ray doses were found to be efficacious.

Some cases ran a course of a few weeks, while others were protracted for several months with exacerbations.

SUMMARY

Thirty cases of infectious eczematoid dermatitis were studied as to age grouping, skin manifestations, allergy, bacterial flora and methods of therapy. In this series no proof of bacterial allergy of eczematous nature was determined by contact testing with organisms obtained.

709 Central Bank Bldg., (Dr. McDaniel).

NOTE.—Since this article was originally written aureomycin given enterally has been found to be a superior therapeutic agent in the treatment of this condition.

GENERALIZED ERUPTION FROM UNDECYLENIC ACID

A. J. REICHES, M.D.
ST. LOUIS

Undecylenic acid, which has been suggested for use in the treatment of psoriasis, neurodermatitis and some forms of arthritis, is among the most recent drugs to be used internally in dermatology. It is interesting to report a generalized cutaneous eruption from the use of undecylenic acid, given in the form of an enteric-coated capsule for a case of psoriasis. The case reported here is apparently the first to be so reported.

REPORT OF A CASE

The patient, a 12 year old girl, was originally seen by me about thirteen months previous to the time of writing, when a diagnosis was made of guttate psoriasis, covering numerous areas of her body. This cleared up under local medication. The patient was seen again on May 20, 1949, because of a recurrence of psoriasis which had started about two months previously. Undecylenic acid, in the form of an enteric-coated capsule of 500 mg., was suggested. Because of the patient's age 2 capsules were to be used three times a day. The patient first took 2 capsules in the early part of the afternoon and again took 2 capsules the same evening. After the use of 4 more capsules the next day a cutaneous eruption began to spread over the body. The lips and eyelids started to swell. By early evening of the second day the eruption covered the entire body. When the patient was seen the following day, which was the third after she had started to take undecylenic acid, there was found on examination a generalized morbillous eruption covering the face, neck, trunk, arms, palms and soles, in addition to edema of the eyelids and lips. There was no adenopathy or subjective symptoms.

The undecylenic acid therapy was stopped after the use of 10 capsules, and no more was given. The eruption began to clear up, first on the legs, arms and back, and the edema of the lips and eyelids disappeared within forty-eight hours. The eruption completely disappeared within seven days.

SUMMARY

A case of cutaneous eruption following the oral use of undecylenic acid is reported.

4500 Olive Street (8).

From the Department of Dermatology, Jewish Hospital.

AUREOMYCIN OINTMENT IN ACNE VARIOLIFORMIS

J. B. HOWELL, M.D.
DALLAS, TEXAS

Experience in one case of extensive and long-standing acne varioliformis suggested that local aureomycin therapy may be effective in managing this disease. Three other patients for whom this diagnosis had been made clinically and whose condition was being managed or controlled satisfactorily on topical ammoniated mercury therapy (5 per cent) were given a trial with aureomycin ointment. They discontinued mercury therapy until recurrence was noted and then compared the efficiency of aureomycin ointment with that of the mercury ointment on previous

trials. The response or clearing of lesions under treatment with aureomycin ointment was as good as under mercury ointment therapy. In another case in which mercury ointment was only partially effective in managing or controlling the eruption, aureomycin ointment seemed to be more effective and brought the eruption promptly under control.

Evaluation of a drug in treatment of a disease in which there are spontaneous remissions is difficult. Acne varioliformis is such a disease, and this factor of spontaneous clearing or remission was taken into consideration in the evaluation. It appears that aureomycin ointment is as effective as ammoniated mercury in managing acne varioliformis. Neither preparation appears to be curative. Relapses are expected after discontinuation of topical therapy. In cases of acne varioliformis in which sensitization to mercury has been acquired aureomycin ointment may be the drug of choice.

None of the five patients have manifested contact dermatitis from aureomycin. Twelve weeks was the longest time that the ointment had been applied continually in any of the cases.

Further confirmation studies are needed. Oral aureomycin therapy alone or in combination with local treatment should be evaluated. Prolonged continuous use of aureomycin ointment to determine its effectiveness as a curative measure should be carried out. Other antibiotics such as bacitracin and streptomycin may be of service in the treatment of acne varioliformis.

ALLERGIC ECZEMATOUS CONTACT TYPE SENSITIVITY OF EQUAL DEGREE TO STREPTOMYCIN AND DIHYDROSTREPTOMYCIN

Report of a Case

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NEW YORK
AND
IRVING H. DISTELHEIM, M.D.
CHICAGO

There have been several reports in the recent literature to show that patients with vestibular reactions to systemic administration of streptomycin can tolerate dihydrostreptomycin. This observation has been taken as evidence of a lower neurotoxicity of the dihydrostreptomycin.[1] Preliminary studies of several patients and laboratory animals indicate that dihydrostreptomycin may also be less toxic to the auditory apparatus and renal system.[2] It therefore appeared to us that it might be of some interest to ascertain whether patients allergic to streptomycin would show equal, less or greater sensitivity to dihydrostreptomycin. This report may throw some light on the foregoing questions. It deals with a case

1. Hobson, L. B.; Tompsett, R.; Muschenheim, C., and McDermott, W.: A Study of Dihydrostreptomycin, Am. Rev. Tuberc. **58**:501-524 (Nov.) 1948. Levin, L.; Carr, D. T., and Heilman, F. R.: The Distribution of Dihydrostreptomycin in Various Body Fluids, ibid. **58**:531-536 (Nov.) 1948. Hinshaw, H. C.; Feldman, W. H.; Carr, O. T., and Brown, H. A.: The Clinical Administration of Dihydrostreptomycin in Tuberculosis, ibid. **58**:525-530 (Nov.) 1948.

2. Edison, A. O.; Frost, B. M.; Graessle, O. E.; Hawkins, J. E., Jr.; Kuna, S.; Mushett, C. W.; Silver, R. H., and Solotorovsky, M.: An Experimental Evaluation of Dihydrostreptomycin, Am. Rev. Tuberc. **58**:487-494 (Nov.) 1948.

of a nurse who exhibited an allergic contact type eczematous dermatitis from professional exposure to streptomycin and in whom patch tests revealed a hypersensitivity to dihydrostreptomycin as well as to the streptomycin itself. The patient, a well trained nurse, had no knowledge of ever having been exposed to dihydrostreptomycin, and all the evidence obtainable indicated that no such exposure had occurred.

REPORT OF CASE

Mrs. A., a 40 year old white nurse, was first seen by us on June 22, 1948, and gave a history of having had a dermatitis of both hands for four months. During this time she also had one episode of concomitant periocular edema. The history further revealed that she had been handling penicillin. Examination at that time revealed an erythematous, weeping, crusted and vesiculopustular eruption involving both hands. Studies for fungi yielded negative results. On July 19 the patient was given patch tests with penicillin (as shown in the accompanying

Patient's Reactions to Various Patch Tests

Date	Substance Tested	Concentration	Reaction
7/19/48	Penicillin solution	500 units/cc.	++
11/26/48	Tyrothricin solution	25 mg./cc.	0
	Tyrothricin ointment	0.5 mg./Gm.	0
	Penicillin solution	500 units/cc.	0?
	Penicillin ointment	1,000 units/Gm.	0?
	Streptomycin ointment	5,000 megm./Gm.	++
	Streptomycin solution	25 mg./cc.	+ to ++
	Trichophytin solution	1:30	0
	Oidiomycin	Undiluted	0
	Ammoniated mercury	3%	0
12/ 9/48	Dihydrostreptomycin	25 mg./cc.	0 to +?
12/11/48	Penicillin solution	500 units/cc.	++
	Streptomycin ointment	5,000 megm./Gm.	+?
1/19/49	Bacitracin ointment	500 units/Gm.	0
	Streptomycin ointment	5,000 megm./Gm.	++
	Penicillin solution	500 units/cc.	0
	Dihydrostreptomycin solution	50 mg./cc.	++
	Aureomycin	50 mg./cc.	0

table) and had a 2 + eczematous type reaction. During the month of August her condition almost cleared on local remedies and abstinence from work. The patient returned on September 2, however, exhibiting a new eruption clinically similar to the first. This time she gave a history of having come in contact with both penicillin and streptomycin on returning to work several days before. In view of this history, a series of patch tests were done. The accompanying table shows the results of all the patch tests with antibiotics and other materials including the test on July 19 after the first eruption and the remainder in the months following her second attack.

SUMMARY AND CONCLUSIONS

While vestibular, aural and renal reactions to systemic administration of dihydrostreptomycin have been reported to be regularly less than those to streptomycin, patch testing indicated, in this particular case at least, that the local allergic eczematous contact type reaction was the same for both drugs. Also of interest in this case were the observed fluctuations of sensitivity to penicillin which at times suggested possible cross sensitivity between penicillin and streptomycin. Patch testing with additional antibiotics as well as trichophytin and oidiomycin yielded no evidence of other polyvalent hypersensitivity or cross reactions in this patient.

999 Fifth Avenue (28).

MICROSPORON LANOSUM INFECTION OF THE EYELASHES

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and
EDWARD H. MANDEL, M.D.
NEW YORK

In view of the paucity of reports of fungous infection of the eyelashes, particularly that caused by Microsporon lanosum, the following observations are considered worthy of note.

REPORT OF A CASE

M. M., a girl 10 years of age, acquired an eruption of the left upper eyelid a few days after a stray kitten was brought into the household. The child was treated by a local physician for chickenpox. Later, new lesions, for which she was given topical medication, appeared on her trunk and face. This therapy was to no avail, and three weeks from the onset the patient appeared at our clinic.

Initial examination of the face, eyelids and chest showed discrete erythematous quarter-dollar-sized patches with peripheral vesiculation. The right eyelashes and adjacent lid presented only an erythematous color change. Under the filtered

Results of Mycologic Studies

Subject	Results of Examination Under Filtered Ultraviolet Radiation	Trichophytin Test		Results of Microscopic Examination of Specimen in Sodium Hydroxide	Culture
		Reading at 15 Min.	Reading at 48 Hr.		
M. M., aged 10	Positive (Eyelashes)	Negative	Positive	Positive	M. lanosum
R. M., aged 4½	Positive (Scalp)	Negative	Positive	Positive	M. lanosum
Kitten	....	....	....	Positive	M. lanosum

ultraviolet radiation about eight hairs in the middle of the eyelid were fluorescent. The right eyebrow presented one of the quarter-dollar-sized patches mentioned above.

The patient's brother, R. M. (4½ years of age), presented a similar eruption of the face, trunk and scalp. This became noticeable shortly after the sister's rash appeared. There was no involvement of the eyelashes. Both patients were treated conservatively with zincundesal (salundek®; zinc undecylenate, 25 per cent; salicylanilide, 5 per cent, and undecylenic acid, 2 per cent, in a carbowax® base) with prompt response.

Mycologic studies were done on the girl, brother and kitten. Data are given in the accompanying table.

COMMENTS

Tinea capitis with involvement of the eyelashes is rather rare. Montgomery and Walzer,[1] reviewing 560 cases of proved M. audouini infection from January

From the New York Skin and Cancer Unit and the Department of Dermatology and Syphilology, Dr. Marion B. Sulzberger, chairman, Post-Graduate Medical School of New York University–Bellevue Medical Center.

1. Montgomery, R. M., and Walzer, E.: Tinea Capitis with Infection of Eyelashes: Report of a Case, Arch. Dermat. & Syph. **46**:40 (July) 1942.

1935 to July 1941 at the New York Skin and Cancer Unit, reported one case of infection of the eyelashes by Microsporon audouini. They also reported the appearance of a circinate lesion located on the right shoulder of their patient's brother. This too was proved to be due to M. audouini.

Since then Silvers [2] reported another case of involvement of the eyelashes due to M. audouini in an 8½ year old boy with an upper and lower lid infection. Two months prior to this the patient presented a lesion on the right cheek which was fluorescent under filtered ultraviolet radiation.

We [3] recently noted another case of M. audouini infection of the eyelashes. Other hyphomycetes that have been isolated from eyelashes include Trichophyton album,[4] Trichophyton asteroides [5] and Trichophyton granulosum.[6]

SUMMARY

A study of the literature suggests that M. lanosum infection of the eyelashes is exceedingly rare.

A case is reported which showed this rare localization.

The results of mycologic and immunologic examinations are presented.

60 Gramercy Park North (Dr. Franks).

30 East Sixtieth Street (Dr. Mandel).

2. Silvers, S. H.: Microsporon Audouini Infection of the Eyelashes, Arch. Dermat. & Syph. **49**:436 (May) 1944.

3. Franks, A. G.; Mandel, E. H., and Sternberg, A. S.: An Endemic of M. Audouini Infection in a Family of Eight Persons, Arch. Dermat. & Syph. **62**:54 (July) 1950.

4. Footnote deleted.

5. Coutela, M. M., and Offret, G.: Un cas de teigne cilio-palpébrale, Bull. Soc. d'opht. de Paris 1936, pp. 402-405.

6. McCarthy, L.: Diagnosis and Treatment of Diseases of the Hair, St. Louis, C. V. Mosby Company, 1940, p. 365.

SIMPLE EFFICIENT METHOD OF EXAMINING SKIN SCRAPINGS FOR FUNGI

MARC ALLEN WEINER, M.D.
WASHINGTON, D. C.

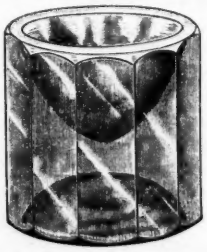
Very often the diagnosis is made of "ringworm," "athlete's foot," dermatophytosis, etc., without the corroboration of a microscopic demonstration of the fungi assumed to be present. Conversely, many cases of fungous infection are undiagnosed because direct examinations are not made. This situation is attributable in part to the physician's inability or unwillingness to perform the requisite examination. Anything which makes this procedure more simple and convenient might induce more physicians to get into the habit of performing microscopic examinations for fungi. It is with this thought in mind that a simple modification of the usual technic is presented.

The usual method of doing a direct examination for fungi consists in swabbing the skin with alcohol, scraping the suspected lesion with a scalpel, catching the

scales on a glass slide (or on paper, and then placing the scales on a slide), adding a drop or two of potassium hydroxide solution and finally placing a cover slip on the material. The mount is then examined microscopically after about 30 minutes.

The only modification of this procedure which I have employed is to catch the skin scrapings in a Dappen medicament glass such as is used by dentists to contain small amounts of medication into which they can dip bits of absorbent cotton. This type of cup is usually ten sided and heavy and has a biconcave internal structure, as illustrated in the accompanying figure. It is available in several colors, but brown seems to be preferable for the use described here, affording a dark background for the pale bits of tissue.

My procedure is as follows: The suspected lesion is wiped with an alcohol sponge to remove possible saprophytic organisms and surface bacteria. When dry, the skin is scraped with a flamed scalpel (no. 10 curved blade), the material falling into the Dappen dish which is held against the skin below the lesion. The residual scrapings on the blade are inoculated onto Sabouraud's medium. If no residuum is present some scrapings are picked up with the blade from the cup and then inoculated. A few drops (three to 20) of 20 to 30 per cent potassium



Dappen medicament glass, actual size.

hydroxide solution are added to the dish, the scales adhering to the sides of the dish thus being washed down to the bottom. An identifying adhesive plaster "label" is attached to both culture tube and dental dish. The latter is covered with a glass slide or small watch glass, to keep out dust and air-borne fungi, and is allowed to stand until it can be examined conveniently. At that time a drop or two of the suspension is transferred from the Dappen dish to a slide by means of a medicine dropper.

If one is in the habit of doing many skin scrapings and time does not permit immediate examination, the several dishes may be examined at the end of the working day or even on the following day. In 24 hours evaporation of the potassium hydroxide solution is negligible, dissolution of keratin is even more complete and the fungi remain clearly visible. Potassium hydroxide crystals do not form as long as drying out is not imminent.

The advantages of this modification are as follows:

1. Any available amount of skin scrapings may be obtained at one sitting.

2. The concentration of scrapings per microscopic field can be controlled simply by varying the amount of potassium hydroxide solution which is added to the Dappen dish.

3. Where suspicion as to a fungus origin is strong even in the face of a negative mount, several more mounts can be made from the same dish for

reexamination. One is occasionally rewarded with a positive finding on the second or third examination, either at the same sitting or at a later time.

4. The time limit for examination of the mount is long—24 hours and longer—whereas with the mount made directly onto a slide one must examine the material within a few hours because of the possibility of crystal formation and drying out of the solution.

5. All scrapings can be examined at one time, either on the day of obtaining the material or on the following day, at the convenience of the examiner.

6. If for some reason the suspension should dry out, the addition of a few more drops of potassium hydroxide solution to the dish restores the suspension to its former state.

SUMMARY

A simple modification of the usual method of examining skin scrapings for the presence of fungi is described, and its advantages are enumerated.

915 Nineteenth Street, N.W. (6).

PHOTOSENSITIZATION INDUCED BY MONOGLYCEROL PARAAMINOBENZOATE

A Case Report

E. M. SATULSKY, M.D.
ELIZABETH, N. J.

The purpose of a sun tan or sun-filtering preparation is to produce a tanning of the skin with a minimum of erythema after exposure to sunlight. Thus, an ideal preparation would be one which filtered out all the light rays shorter than 3,200 angstrom units and allowed the longer ones to pass. Despite the wide use of many organic chemicals to produce this effect, dermatitis from sun tan preparations has rarely been reported.

Paraaminobenzoic acid and certain of its esters have been shown to be excellent filtering agents against the erythema-producing part of the sunlight spectrum, i. e., rays of 2,500 to 3,200 angstrom units.[1] Because of its excellent filtering capacity, its lack of odor and its lack of staining properties, monoglycerol paraaminobenzoate (an ester of paraaminobenzoic acid) has been incorporated in a number of commercial sun tan preparations. Baer and Meltzer[2] reported a case of allergic eczematous contact type hypersensitivity to this monoglycerol ester and have cited a number of interesting cross sensitizations to various other important chemicals.

The purpose of this report is to record a case of photosensitization induced by monoglycerol paraaminobenzoate. This is not ordinary photosensitization but a demonstration that one skin may be allergically more susceptible to photosensi-

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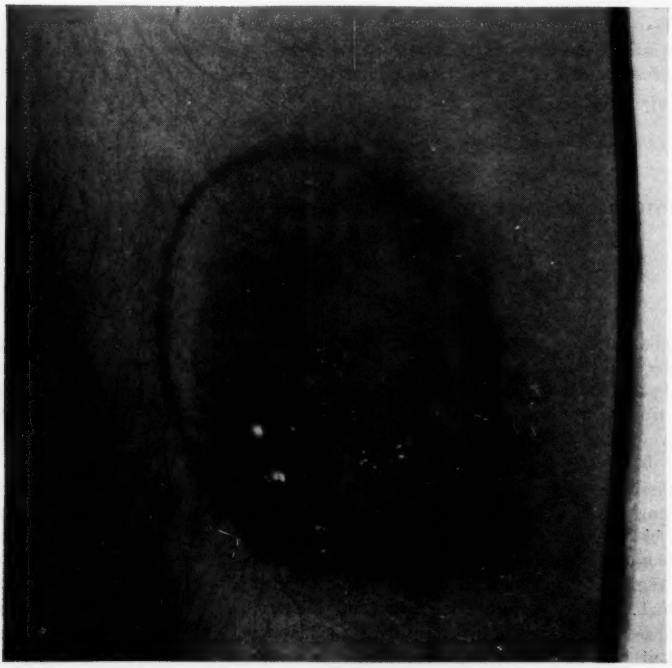
1. Rothman, S., and Rubin, J.: Sunburn and Para-Aminobenzoic Acid, J. Invest. Dermat. **5**:445, 1942. Rothman, S., and Henningsen, A. B.: The Sunburn-Protecting Effect of Para-Aminobenzoic Acid, ibid. **9**:307, 1947.

2. Baer, R. L., and Meltzer, L.: Sensitization to Monoglycerol Para-Aminobenzoate, J. Invest. Dermat. **11**:5, 1948. Meltzer, L., and Baer, R. L.: Sensitization to Monoglycerol Para-Aminobenzoate: A Case Report, ibid. **12**:31, 1949.

tization than another. This concept has been demonstrated in the past in regard to photosensitization with sulfanilamide, but to my knowledge it has never been described with monoglycerol paraaminobenzoate.

REPORT OF A CASE

S. L., a male student aged 25 years, was first seen by me on July 19, 1949. About two weeks prior to this date, he spent a week end at the beach and in order to protect his skin from the sun he applied a widely used commercial sun tan lotion. The following day he noted severe generalized itching and the development



Reaction following the application of sun tan lotion to the forearm, which was then exposed to sunlight.

of an eruption which started on the forearms and rapidly spread to involve all parts of his body except the areas covered by bathing trunks. The involved areas coincided with the parts which had been covered with the lotion. The patient applied calamine lotion and tried to treat himself until the date of the first consultation. He presented a diffuse generalized erythrosquamous dermatitis with numerous scattered areas of tiny vesicles. Both legs and knees were edematous and presented hemorrhagic vesicles of various sizes and scattered purpuric patches. There were sharp lines of demarcation at the bathing trunk area. In this area the skin appeared normal. There was severe exfoliation of the skin on the hands, forearms

and thighs. The skin over the anterior part of the abdominal wall and neck showed fading erythema. The rest of the physical examination was noncontributory. Under treatment which consisted of bed rest, avoidance of soap and water, starch baths, application of a soothing emulsion and the administration of antihistamine preparations by mouth the condition cleared completely.

The patient was next seen on Aug. 11, 1949. His skin was then entirely normal, and he had no complaints. A patch test with the sun tan lotion was applied to his back. He was instructed to apply this lotion to the flexor surfaces of the forearms and expose these parts to the sunlight. In 48 and 72 hours the reaction to the patch test was negative. On the forearms, however (photograph), in the areas where the lotion had been applied there were two large edematous, erythematous, sharply demarcated patches. These areas were hot and pruritic. On the right forearm there were several large bullae and vesicles; the left forearm was similarly involved but to a lesser degree. On the finger tips, which had also been exposed to the sunlight, there were scattered erythematous and vesicular patches where contact had been made when the lotion was applied.

On Sept. 13, 1949, the same lotion was applied in the office to both forearms and they were exposed to ultraviolet radiation at 30 inches (76 cm.) for 1½ minutes. In 12 hours the patient complained of severe itching, and in 48 hours there were two large erythematous and vesicular patches coinciding exactly with the areas where the lotion had been applied.

Through the courtesy of the manufacturer the eight ingredients of this sun tan lotion were obtained in the concentrations in which they are present in the finished product. The patient was then given patch tests on his back with each individual ingredient and with the lotion itself, and the individual ingredients were applied on the forearms, which were then exposed to ultraviolet radiation at 30 inches for 1½ minutes.

The patch tests on the back all gave negative reactions in 48 and 72 hours. The areas on the forearms also gave negative reactions except the area which had been painted with the monoglycerol ester of paraaminobenzoic acid. This area was sharply demarcated and was edematous, vesicular and extremely erythematous.

COMMENT

After the tests were completed, further questioning revealed that several years ago, while in the Army, the patient had taken sulfathiazole as prophylaxis. He would not consent to further testing to determine the possibility of cross sensitization. As noted by Meltzer and Baer, mention should be made of the possible significance of the ingestion of paraaminobenzoic acid as a vitamin factor in foods. In the present case there is no history of any sensitivity to foods, but the minute amounts of paraaminobenzoic acid ingested might be capable of acting as a sensitizing agent.

CONCLUSIONS

This is a case report which demonstrates photosensitization induced by the monoglycerol ester of paraaminobenzoic acid. It demonstrates that there may be an allergic difference in susceptibility to photosensitization on the part of different persons or that one skin is allergically more susceptible to photosensitization than another.

737 North Broad Street.

FAILURE OF AUREOMYCIN HYDROCHLORIDE THERAPY IN WARTS

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PITTSBURGH
and
STANTON M. HARDY, M.D.
Medical Director, Lederle Laboratories Division, American Cyanamid Company
PEARL RIVER, N. Y.

After observation of an almost specific-like response of the condition of a 1 year old child, who presented multiple molluscum contagiosum lesions over the diaper-covered area, to treatment with aureomycin, just as originally reported by Guy and associates,[1] and following the suggestion of these authors that the virucidal activity of this same antibiotic be explored in the treatment of ordinary warts, we undertook such evaluation in 10 patients.

Results of Aureomycin Hydrochloride Therapy for Warts

Case	Patient	Sex	Age	No. of Warts	Location	Results
1	A. S.	F	18	3	Plantar	Excellent
2	E. A.	F	36	7	Face	Excellent
3	E. J.	F	16	26	Hands and knees	Unsatisfactory
4	K. McC.	F	6	8	Anterior nares	Unsatisfactory
5	F. D. M.	M	12	3	Fingers	Unsatisfactory
6	L. T.	M	21	1	Fingers	Unsatisfactory
7	D. G.	M	17	44	Hands	Unsatisfactory
8	G. H.	F	34	4	Hands	Unsatisfactory
9	C. H.	F	7	6	Hands	Unsatisfactory
10	E. H.	M	9	3	Hands	Unsatisfactory

The unreliability and the vagary in the behavior of warts under any kind of treatment was again demonstrated in this small series, as the first and the second patients were seemingly cured as a direct result of the ingestion of aureomycin hydrochloride, while the other eight, though on exactly the same treatment, showed absolutely no response.

Each patient in this series had treatment-resistant warts, as all had had one or more accepted forms of treatment previously. In none was the condition of less than one year's duration.

The treatment consisted of the ingestion of 250 mg. of aureomycin hydrochloride three times a day for a period of 14 days. None of the patients had to stop taking it, although one complained of nausea on and after the tenth day.

The first patient was a student nurse; she had three plantar warts. At the end of one week, on the first day of the post-treatment inspection, there was a decided diminution in the size of the warts, and also the callus about each wart was exfoliating. At the end of the 14 day treatment period no sign of the warts or the callus remained.

1. Guy, W. H.; Jacob, F. M., and Guy, W. B.: Aureomycin in Molluscum Contagiosum, Arch. Dermat. & Syph. **60**:629 (Oct.) 1949.

The second patient, a pregnant woman of 36 who presented seven unsightly warts on her face, had a similarly good response.

Then followed the failures in the next eight patients. The last three were members of the same family, a mother, daughter and son.

Like most therapeutic procedures, aureomycin hydrochloride failed to give satisfactory results in the treatment of ordinary warts.

GRANULOMA FISSURATUM HEALED BY PENICILLIN TROCHES

COLEMAN MOPPER, M.D.
AND
JAMES R. ROGIN, M.D.
DETROIT

Granuloma fissuratum was distinguished as a clinical entity by Sutton Jr.[1] in 1932, and since then a small number of cases have been reported. Sutton described the lesion as a circumscribed, firm, whitish, fissured, granulomatous new growth occurring in the labioalveolar fold. The lesion is discoid, smooth, rounded and slightly raised, being approximately a centimeter in diameter, lacking an inflammatory areola and folded similarly to a bent coin, so that the fissure in the bend is continuous at both sides with the labioalveolar sulcus. Symptoms are slight. Sutton's two original cases involved the superior labioalveolar sulcus, but other cases have been described subsequently involving the inferior sulcus. The etiology is unknown, but several authors have incriminated dentures as an etiologic contributing factor, even though the dentures did not touch the lesion; streptococcic origin is also postulated. Sutton classified these lesions in the granuloma pyogenicum group. For treatment, Sutton and Sutton[2] stated that excision is curative but that perhaps conservative methods may be beneficial, as applications of tincture of iodine cured an early lesion. Greenbaum,[3] in 1933, reported two cases, one of which disappeared after the institution of proper oral hygiene and adjustment of artificial dentures, although the dentures did not touch the lesions. Ormsby and Montgomery's[4] textbook stated simply that "the treatment of this condition consists of surgical extirpation." Andrews[5] advocated any destructive procedure but favored electrodesiccation followed by local antiseptic measures.

As these three textbooks of dermatology seem to have emphasized the necessity of destructive procedures for treatment of this benign condition, it was deemed worth while to report the successful use of penicillin troches as treatment in the following case.

From the Department of Dermatology, Wayne University Medical School, Dr. Loren W. Shaffer, professor.

1. Sutton, R. L., Jr.: A Fissured, Granulomatous Lesion of the Upper Labio-Alveolar Fold, Arch. Dermat. & Syph. **26**:425 (Sept.) 1932.

2. Sutton, R. L., Sr., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 1486.

3. Greenbaum, S. S.: Granuloma Fissuratum (Sutton), Urol. & Cutan. Rev. **37**:841 (Dec.) 1933.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, p. 1430.

5. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 3, Philadelphia, W. B. Saunders Company, 1946, p. 267.

REPORT OF A CASE

M. M., a fairly well nourished white woman aged 65, was seen on Nov. 3, 1949. She stated that a sore on her upper gum and lip had been noticed about three weeks previously and had been treated by her family physician with local applications of silver nitrate and methylrosaniline chloride (gentian violet) with very little benefit. She had not used her dentures during the past three weeks, except when eating. Examination revealed a fissured ulcerative lesion on the upper margin of the gum at the junction of the buccal mucosal surface of the left side of the upper lip. The ulcerating lesion in the superior alveolar sulcus was approximately 1.5 cm. long and 1 cm. wide, being folded back on itself as a bent coin is. The base of the ulcer was whitish and showed no evidence of pyogenic inflammation. A diagnosis of granuloma fissuratum was made, and penicillin troches of 5,000 units each were prescribed to be used every two hours while the patient was awake. Saline gargles several times daily were also prescribed. This patient was seen 10 days later, and at that time the ulcer was vastly improved and a decrease of 90 per cent from the original size was estimated. As the patient complained of a sore tongue and on examination the tongue was observed to be smooth, slick and suggestively beefy red, the taking of a multiple vitamin B capsule was prescribed, along with continuation of use of the penicillin troches. The patient was seen again two weeks later, at which time the original granulomatous and ulcerating lesion was entirely healed, the tongue was not sore and there was no evidence of the formation of a black hairy tongue, such as has been reported previously in the literature to follow the use of penicillin troches.

SUMMARY

A case of granuloma fissuratum which responded favorably and rapidly to the use of penicillin troches is reported.

It seems advisable that in future cases conservative measures of treatment be tried before destructive methods are instituted.

INCIDENCE OF PSORIASIS

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BALTIMORE

Recently Dr. Richard Sutton Jr.[1] wrote a note on the incidence of psoriasis. In his note he stated that he found the incidence of psoriasis to be 0.2 per cent. He expressed the opinion that Gahan's[2] figure of not less than 1 per cent is too high. He also stated that psoriasis is far down on the list of common diseases of the skin in contrast to its position second only to acne in order of frequency in the list of Bereston and Ceccolini.[3]

1. Sutton, R. L., Jr.: Incidence of Psoriasis, Arch. Dermat. & Syph. **58**:740 (Dec.) 1948.

2. Gahan, E.: Incidence of Psoriasis Among the Population at Large, Arch. Dermat. & Syph. **48**:305 (Sept.) 1943.

3. Bereston, E. S., and Ceccolini, E. M.: Incidence of Dermatoses in Twenty Thousand Army Induction Examinations, with Note on Syphilis with Negative Serologic Reactions, Arch. Dermat. & Syph. **47**:844 (June) 1943.

I should like to point out the fact that in the list of Bereston and Ceccolini there were 55 cases of psoriasis in 20,000 men, which is an incidence of 0.27 per cent, a figure which varies by only 0.07 per cent from Dr. Sutton's own figure of 0.2 per cent.

The fact that psoriasis was second in frequency and not farther down on the list may have been due to sex factors, seasonal factors or geographic factors, as the men examined were mostly from western Washington state, an area noted for lack of sunshine. Crocker [4] placed psoriasis fourth in frequency on his list, and Bulkley [5] placed it third on his list, while the other authorities place it about sixth or seventh on their lists. I should like to state that eczema on most of the lists in the literature includes varicose eczema, neurodermatitis disseminata and neurodermite, while in the list of Bereston and Ceccolini these were separately classified, eczema thus being dropped out of second place and psoriasis becoming second instead of third. A careful study of the paper will reveal these facts: 1. Psoriasis in 20,000 inductees had an incidence of 0.27 per cent, which varies only by 0.07 per cent from the figure of 0.2 per cent given by Dr. Sutton. 2. Sex, seasonal, geographic and statistical factors placed psoriasis second in frequency of skin diseases in 20,000 inductees.

2406 Eutaw Place (17).

4. Crocker, H. R.: Diseases of the Skin, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 1401.

5. Bulkley, L. D.: Manual of Diseases of the Skin, ed. 4, New York, G. P. Putnam's Sons, 1898, p. 41.

INFLUENCE OF LOCAL APPLICATION OF ADRENAL CORTICAL EXTRACT ON HAIR GROWTH IN THE HUMAN

RHODA GRANT, Ph.D.
THEODORE CORNBLEET, Ph.D., M.D.
and
M. I. GROSSMAN, Ph.D., M.D.
CHICAGO

Baker and Whitaker [1] reported inhibition of growth of hair follicles, atrophic changes in epidermis, dermal changes and reduction in sebaceous glands in rats following direct application of adrenal cortex preparations to the skin. Changes were similar to those seen after parenteral injection of adrenocorticosterone. The ability to produce this effect was attributed to the 11-oxysteroids from the adrenal cortex.

In this present study, five human subjects, one female and 4 male, applied 0.6 cc. of adrenal cortex extract [2] in 25 per cent alcohol to an area 30 mm. square

From the Departments of Clinical Science and Dermatology, College of Medicine, University of Illinois.

1. Baker, B. L., and Whitaker, W. L.: Anat. Rec. **102**:333, 1948.

2. The adrenal cortex extract used in these studies was supplied by Dr. H. F. Hailman of the Upjohn Co., who informed us that it was assayed by the glycogen deposition method in the rat and found to contain 5 units per cubic centimeter, which is equivalent to 1 mg. of 17-hydroxy-11-dehydrocorticosterone (cortisone; compound E) per cubic centimeter.

on the ventral surface of the thigh daily, using as a control 25 per cent alcohol on the corresponding area on the other leg. In two of the subjects the areas were shaved. The experiment lasted 14 weeks in the males but was ended in the other case at 9 weeks. In all cases the number of hairs in the test areas were counted at the beginning of the tests and at intervals of seven to 10 days thereafter.

RESULTS

No significant difference in hair counts was found between control and extract-treated areas in any of the subjects. No apparent differences in the average length of hairs in the two areas occurred.

Biopsies of control and treated areas were taken at the end of nine weeks in one case (the female subject) and examined histologically for signs of inhibition, with negative results.

In the remaining four subjects, tests for skin reactions to intracutaneous injections of histamine (1 : 1,000), epinephrine (1 : 1,000) and acetylcholine (1 : 100) were made at the end of the period of application (14 weeks). In three of the subjects the histamine flare on the extract-treated area was less intense than that on the control area. Reactions for the other agents were the same on both legs, i. e., the sweating response, piloerection and vasoconstriction to epinephrine and the muscarine-like and axonreflex pilomotor and sweating effects of acetylcholine.

Several patients afflicted with various forms of hypertrichosis were treated with local applications of this adrenal cortex extract for periods extending up to three months. No effect was noted.

From these experiments no evidence was found in support of the view that adrenal cortex extract containing 11-oxysteroids and other cortical steroids inhibits growth of skin structures in the human.

SUMMARY

In contrast to the report of Baker and Whitaker on rats, in human subjects local application of an adrenal cortex extract for 14 weeks failed to restrain hair growth.

PRESSURE RING FOR HEMOSTASIS

EDMUND N. WALSH, M.D.
TEMPLE, TEXAS

Hemorrhage during and after a punch biopsy of the skin is often profuse and may interfere both with the removal of the specimen and with subsequent desiccation. The idea of a pressure ring for controlling bleeding was first suggested by a drawing of such an instrument in Andrews' "Diseases of the Skin," [1] but none was available. A homemade wire ring proved to be so useful that the instrument shown here was designed and has been prepared by one of the instrument houses (figure).

The ring is made of stainless steel with a smooth curved surface for pressure on the skin. The bar attaching the ring to the handle is placed at a 45 degree

From the Department of Dermatology, Scott and White Clinic.

1. Andrews, G. C.: Diseases of the Skin, for Practitioners and Students, ed. 3, Philadelphia, W. B. Saunders Company, 1946, p. 54.

angle so that pressure can be easily applied and so that use in the mouth or in a depressed area such as that about the inner canthus of the eye may be facilitated. The flat corrugated aluminum handle allows a firm grip and good control with a minimum of effort. Rings 10 and 12 mm. in inside diameter have been found most suitable for the usual 4 to 6 mm. punch biopsy.

Bleeding during and after the biopsy procedure is readily controlled by the pressure ring. In addition to controlling bleeding, the ring holds and steadies the tissues so that a better cut can be made with the punch. This is particularly helpful in dealing with loose, thin or atrophic skin such as is often found near

Pressure ring for hemostasis.

the eye and with old or emaciated persons for whom, because of the mobility and delicacy of the skin, punch biopsies are often unsatisfactory. After the cut with the punch is made, pressure from the ring causes the biopsy plug to protrude above the surface, where it is more easily grasped with small forceps and excised with small curved scissors. The ring is so thin (1.5 mm.) that it does not interfere with this procedure. Use of the instrument at the time the specimen is removed necessitates the help of an assistant, but the operator can hold it himself while using the punch and when controlling bleeding during desiccation.

My associates and I have found the instrument to be very useful and feel that it is worth reporting since, as far as could be determined, no similar instrument is in general use.

Correspondence

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY

To the Editor:—It was my good fortune to attend the annual meeting of the British Association of Dermatology and Syphilology held at Edinburgh from July 13 to 15 this past summer. The meeting was conducted by Dr. Robert Aitken, president, with Dr. J. E. M. Wigley, London, as secretary and Dr. G. A. Grant Peterkin, local secretary. The sessions were held in the Department of Dermatology (Prof. G. H. Percival) of the Royal Infirmary and included four half days of programmed papers and a half day clinical meeting. One afternoon was devoted to recreation, and all three evenings were occupied with lighter gatherings. The attendance was about 75 members and guests. The Scots cannot be topped in hospitality and entertainment.

The first day, Thursday, July 13, after a preliminary business meeting, was given over to a symposium on "The Endocrines in Dermatology." The program was opened by Prof. D. M. Dunlop, London, who gave a concise account of the medical background of the problem. His talk was followed by that of a second guest speaker, Dr. MacGregor, who supplied comments on the gynecologic relationships. The final and principal speaker was Dr. H. W. Barber, who developed the theme dermatologically with precision and completeness. After lunch at the University Union—where we ate thereafter each noon—the general discussion was opened. The final paper of the day was given by Brian Russell on the treatment of lupus vulgaris with calciferol. A tea at the hospital concluded the afternoon. Early that evening we were received by the Lord Provost at Edinburgh at a reception in the Civic Chambers.

The second morning was given over to a spirited discussion of the pemphagoid dermatoses, led by Professor Percival. Other discussers, both formal and informal, were Rook, Whimster, Peterkin and Bettley. Professor Dupont, a guest from Belgium, and others from the floor carried on discussion in a lively fashion. During the noon recess, Lemuel Ereaux, Louis Forman and I took the opportunity of climbing about Edinburgh Castle—practically my sole chance of sight-seeing about the city. The afternoon was divided between golf and a bus trip. The latter was a pleasant tour of the neighboring countryside with several stops at the more interesting points, with finally the customary—and refreshing—tea at North Berwick. That evening was the annual dinner of the Association. Given an adequate meal with the appropriate wines, the British need to import no outside entertainment. The toastmaster inspired sprightly and effective responses from among the members.

The session on Saturday opened with a continuation of the discussion of the previous day's papers with Professor Percival giving the final rebuttal in easy and tolerant phrases. Papers by Dr. Hannay on pseudoxanthoma elasticum and by Dr. MacCollum on generalized herpes zoster concluded the schedule of formal papers. The clinical session on the final afternoon included the presentation of some 25 extremely interesting cases as well as several exhibits. To the surprise and great delight of all, Dr. Parkes Weber was able to make an appearance. Inasmuch as he was convalescing from a fractured hip, this was no easy chore for this venerable member. The discussion which followed the case presentations was characterized by the expeditious manner in which Dr. Aitken conducted it as chairman. Discussion was carried on with dispatch so that only the more provocative or problem cases were commented on. The character of the chairmanship and skilful conduct of the meeting are commended in general to all similar meetings.

Most of the members and guests left Edinburgh late on Saturday evening after the president's reception although some were able to stay over Sunday to take advantage of Dr. Aitken's invitation for a day's motor cruise on the Clyde.

After the meeting I returned to London for an additional week of holiday. Visits to St. John's Skin Hospital, Guy's and Bart's were of high interest. More of the generous British hospitality followed, and it was a pleasure to meet again Dr. MacKenna, Dr. Forman, Sir Archibald Gray, Dr. McLeod, Dr. Mitchell-Heggs and my fellow North American, Lemuel Ereaux. Dr. A. H. Harkness, venereologist and a correspondent friend of Herman Beerman, was most cordial and went to considerable effort to make my stay in London a memorable one. All mentioned their many dermatologist friends in the United States and sent numerous greetings by name. So many were included that I have been able to transmit but a small portion of the messages. The Association is planning and looking ahead with anticipation to the International Meeting to be held in London in 1952 and extends a warm invitation for our joint participation.

I left by way of Ireland, with a short stay in Dublin. Here I met Dr. Bethel Solomons Jr., a gracious and complete host. With him I visited several Dublin dermatological wards and clinics. This portion of my trip was much too short, but plane schedules had to be met, and so to Limerick, Shannon and home.

CAPTAIN ROBERT L. GILMAN (MC), U. S. N.

News and Comment

GENERAL NEWS

Manhattan Dermatological Society Plans Fiftieth Anniversary Celebration.—On Tuesday, Nov. 21, 1950, the Manhattan Dermatological Society will celebrate its Golden Anniversary. A special meeting and a special dinner will be held on that date.

American Dermatological Association, Inc., to Hold Prize Essay Contest.—The American Dermatological Association, Inc., is offering a prize of $300 for the best essay submitted, not previously published, of original work relative to some fundamental aspect of dermatology or syphilology. The purpose of this contest is to stimulate younger investigators to original work in these fields.

Manuscript, typed, in English and with double spacing as for publication, together with illustrations, charts and tables are to be submitted in triplicate not later than Feb. 1, 1951, and should be sent to Dr. Louis A. Brunsting, Secretary, American Dermatological Assoication, Inc., 102-110 Second Avenue S.W., Rochester, Minn.

Competition in this prize contest is open to scientists generally, not necessarily physicians.

The award will be made by a committee of judges selected to pass on the essays by the Research Aid Committee of the American Dermatological Association, Inc., and the decision of the judges will be final. This contest is planned as an annual one, but in any year that no paper worthy of a prize is offered, as determined at the discretion of the Research Aid Committee and judges, the award may be omitted.

The prize-winning candidate may be invited to present his paper before the annual meeting of the American Dermatological Association, Inc., with expenses paid, in addition to receiving the $300 prize.

The next annual meeting of the Association will be the Diamond Jubilee Observance of its founding and will be held May 23 to 26, 1951, at the Homestead, Hot Springs, Va.

Further information regarding the essay contest may be obtained by writing to the Secretary of the Association.

Sigmund Pollitzer Lectureship.—Lectures of the Sigmund Pollitzer Lectureship, established by Mrs. Sigmund Pollitzer in honor of her late husband, will be held under the aegis of the New York University Post-Graduate Medical School. The first Pollitzer Lecturer was Dr. Udo J. Wile, professor emeritus of dermatology and syphilology and former dean of the School of Medicine of the University of Michigan, who spoke Oct. 5, 1950, on "Cutaneous Medicine in the Medical Curriculum."

Obituaries

FRED WISE, M.D.

1881-1950

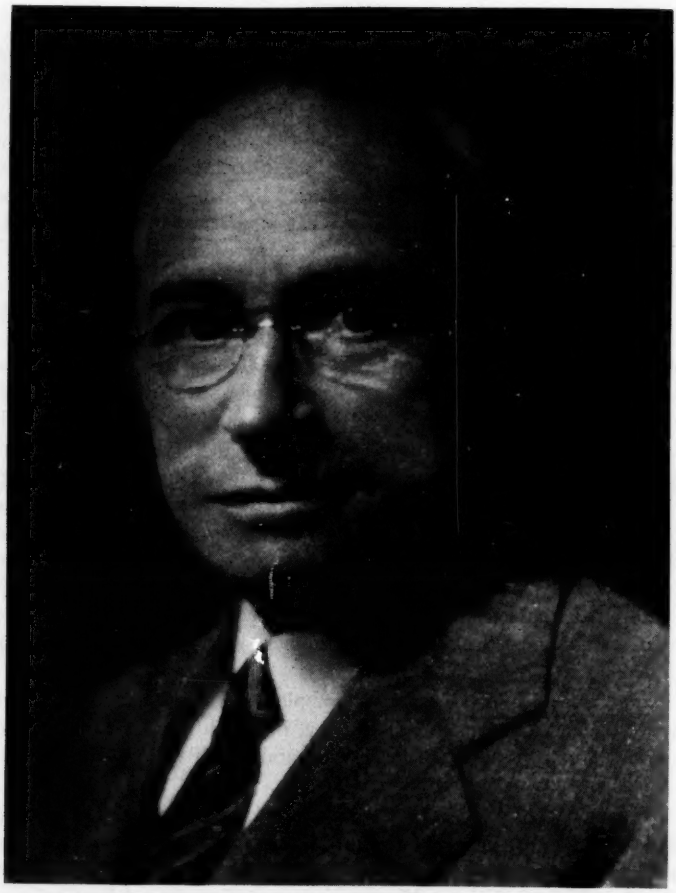
Fred Wise died on July 26, 1950, in the Memorial Hospital, New York, after a long illness. Surviving are his widow, nee Leone Scott, whom he married on Sept. 7, 1913 in Arlington, N. J., and two sisters, Mrs. Joseph Meyer and Mrs. Laura Rice. In the archives of the American Dermatological Association, New York city is given as his place of birth, but his sisters stated that he was born in Miskolcz, Hungary, on Oct. 3, 1881, and, also, that he arrived in this country as an infant with his father, Morris Wise, a successful merchant, and his mother, the former Regina Klein.

Wise's entire education was obtained in New York city—first in the elementary and high schools and then at the College of the City of New York, from which he graduated in 1900; he received his medical degree from the College of Physicians and Surgeons of Columbia University in 1904. During the next year he was resident physician in the New York Skin and Cancer Hospital, one of the few places in this country at the time where a training in dermatology and syphilology could be obtained. At the termination of this residency in 1905 he was appointed clinical assistant and radiotherapist in the same institution. a position that he held until 1909, at which time there was a conflict of ideas between his chief, the late Dr. George Henry Fox, and the director. the late Dr. L. Duncan Bulkley, which resulted in the resignation of the former. Characteristically Wise, together with Dr. Howard Fox. resigned.

As soon as his residency was completed, Wise began the private practice of dermatology and syphilology, in which he was very successful, which was continued until his death and which will be continued by his associate, Dr. Frederick Reiss.

Between 1909 and 1913 Wise served as clinical assistant in urology and dermatology in the German Hospital and as instructor in dermatology in the New York Post-Graduate Medical School. In 1913 he was appointed chief of clinic at Mount Sinai and Beth Israel hospitals and attending dermatologist at Montefiore Hospital, which position he held for many years.

In 1909 Wise accepted an appointment, seemingly of little importance at the time, but which was to have a profound influence on his career. The appointment was that of clinical assistant in Dr. Fordyce's department in the New York University–Bellevue Medical College (now



FRED WISE, M.D.
1881-1950

the College of Medicine, New York University–Bellevue Medical Center). One year later, Dr. Fordyce transferred to Columbia University as professor of dermatology and syphilology in the College of Physicians and Surgeons and Vanderbilt Clinic. It was fortunate that Fred, like me, without hesitation went along with our beloved chief, who was our incentive and benefactor and who provided opportunities and the encouragement for us to take advantage of them. In a short time a group was formed consisting of Fred Wise, Isadore Rosen, David Satenstein and Max Scheer, a group that worked over the many years harmoniously, loyally and unselfishly. This original group eventually developed into an organization of 120 dermatologists. One year after Dr. Fordyce's death (1926) this group and about 40 other members of Dr. Fordyce's staff transferred to the New York Post-Graduate Medical School and Hospital, and in 1932 they became the original staff of the New York Skin and Cancer Unit. Before the above-mentioned transfer, Wise had climbed into the professorial group, having become assistant professor of clinical dermatology. He received a similar appointment in the Post-Graduate Medical School.

When, in 1932, the New York Post-Graduate Medical School and Hospital affiliated with Columbia University and the Stuyvesant Square Hospital (formerly the New York Skin and Cancer Hospital) affiliated with the New York Post-Graduate Medical School and Hospital, the departments of dermatology of both institutions combined to form the New York Skin and Cancer Unit. In the new organization Wise received appointments as associate professor of clinical dermatology and chief of clinic, which appointments he held until he retired in 1947, at which time he was made consultant. He was a major factor in the success of the institution which is now the Skin and Cancer Unit of the New York University–Bellevue Medical Center.

The annual staff dinner of the New York Skin and Cancer Unit, held on March 16, 1946, was a special affair partly in honor of Wise, at which he received many verbal tributes and a handsome engraved gold watch.

Wise was past president of the American Dermatological Association, the New York Dermatological Society and the Manhattan Dermatological Society and past chairman of the Section on Dermatology of the American Medical Association, the Medical Society of the State of New York and the New York Academy of Medicine. In addition, he was an active member of the following local and national scientific bodies: the American Urological Association, New York County Medical Society, New York Society of Dermatology and Genito-Urinary Surgery (defunct), New York Physicians' Association, Alumni Society of the New York Skin and Cancer Hospital, American Academy of Dermatology and Syphilology and the Society for Investi-

gative Dermatology. He resigned from the New York and Manhattan Dermatological Societies in 1947, at which time he was made an honorary member of each. He was corresponding member of the dermatological associations of Hungary, France, Argentina, Brazil, Cuba and Italy.

Wise was an excellent and prolific writer. Alone, and in collaboration with colleagues and students, he contributed about 120 articles to dermatological literature, many of which, even those published 20 or more years ago, are still cited in national and foreign journals. A bibliography of his writings is comprehensive, embracing such topics as rare and uncommon diseases, common diseases with unusual manifestations, physical medicine, conventional therapy, clinical dermatology, histopathology, laboratory observations, education and many aspects of syphilis. His literary style was concise and plain and therefore very readable and easily digested. His first article was published in 1906, when he was 25, one year after his residency in the New York Skin and Cancer Hospital. His last-published article appeared in 1948, but it was not the last one he wrote (delayed publication); his last-written article was a tribute to me which appeared in the *Journal for Investigative Dermatology* (**8**: 276-280 [June] 1947). Little did we know then that in a few years I would be writing this memorial to him.

Wise was associate editor of the *Journal of Cutaneous Diseases* (now the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY) from 1914 to 1919. In 1921 he gave invaluable assistance by reading the manuscript, galley and page proofs of the first edition of my book "X-rays and Radium in the Treatment of Diseases of the Skin"; he contributed a chapter to a later edition.

With Marion B. Sulzberger as associate editor, Wise edited the "Year Book of Dermatology and Syphilology" from 1931 to 1943. This book, previously edited by Dr. Oliver S. Ormsby, has always been considered a most valuable text by dermatologists everywhere.

Being an exceptionally able teacher of practical dermatology and always willing to help students individually or collectively, Wise was always very popular among the matriculates.

Wise was among the first to employ roentgen rays for the treatment of skin diseases in this country, and from 1905 until 1909 he gave most, if not all, of the roentgen ray treatment at the New York Skin and Cancer Hospital. His early articles dealt with this subject. Like most roentgen ray pioneers, he suffered some radiation injury, which he accepted philosophically, as he did all adversities.

Much time was devoted by Wise to the reading of dermatological literature in English, French and German, which occupation, together with a retentive memory, provided him with an unusual knowledge of rare and uncommon diseases of the skin.

While the fact was not generally known, Fred had not enjoyed perfect health for many years, but he never permitted physical incapacities to interfere, except for short intervals, with work, duties and pleasures.

Fred had a number of hobbies, among which were riding saddle horses; trap shooting, at which he won a number of prizes, and hunting game birds, mostly duck, pheasant and quail. He was an almost insatiable reader of well known books on hunting, exploration, adventure and travel. Finding enjoyment in travel and sight-seeing, he had visited most parts of the United States and Canada and also Mexico, Cuba and several European countries. Having a liking for the semiprimitive, he, Mrs. Wise and I spent several weeks together in the Selkirks and Canadian Rockies camping, climbing, hiking and horseback riding. He and Mrs. Wise took a long pack train trip through New Mexico and Arizona and across the Grand Canyon into and through southern Utah. In Arizona they visited the Navajo reservation and obtained interesting moving pictures of Navajo dances.

I knew Fred Wise for 45 years, and I never heard him say one derogatory or unkind word about any person; I have never heard an unkind word about him. He was lenient, tolerant, broad minded, modest, loyal, generous and quite shy. Because he was undemonstrative, his good sense of humor was to some extent hidden. All who were fortunate enough to know him respected, admired and liked him.

Not a single position or honor received by Fred was acquired by request or through favoritism—rather, his success was the result of ability, hard work, loyalty and sterling character. Possessing normal temperament and an even disposition, he was a good companion and a sincere friend.

Our specialty has lost one of its most loved, useful and outstanding members. Those of us who worked in close association with him over the years feel that our life has been enriched through knowing him so well, and the memory of his quiet, appealing personality and his friendship will remain with us always.

GEORGE M. MACKEE

Society Transactions

CLEVELAND DERMATOLOGICAL SOCIETY

Emerson Gillespie, M.D., *President*
Herbert H. Johnson, M.D., *Secretary*
Gerard A. De Oreo, M.D., *Reporter*
Sept. 22, 1949

Sarcoidosis: Improvement Following Treatment with Vitamin D_2; Diabetes Mellitus. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and Dr. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

Sarcoidosis: Improvement Following Treatment with Vitamin D_2. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

DISCUSSION

DR. J. R. HASERICK: The results from therapy have been excellent. The surprising thing is that neither patient had any untoward reaction to vitamin D_2. Curtis has noted that patients with sarcoidosis have a tendency to react to vitamin D_2. My associates and I have had 3 cases of sarcoidosis in which there was extreme hypervitaminosis D within three weeks after such therapy began. One patient manifested hypercalcemia (17 mg. per hundred cubic centimeters) in twelve days, in spite of previous studies to rule out kidney disease and hypertension, for example.

DR. A. E. WALKER: We have had 3 or 4 other patients in the clinic, aside from these 2, treated with the same dosage of vitamin D_2, and they have had no untoward reactions. They were all Negroes; I do not know whether that fact makes any difference.

DR. H. N. COLE: The first patient had an unusual type of reaction. Apparently she never had had diabetes, and then when she was under this therapy there developed a high blood sugar. It reached such enormous heights that we were rather disturbed, and it has persisted even though treatment was discontinued.

DR. J. J. STEWART: The disturbing thing was that we had followed this patient with weekly urinalyses and at no time until just about four weeks ago was there glycosuria.

Lichen Planus: Lichen Planopilaris. Presented by Dr. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

W. C., a Negro woman aged 34, was first seen by us in January 1949, complaining of an eruption which first appeared around her wrists four months prior to her visit. Severe itching accompanied the appearance of the lesions, and they gradually spread to involve the thighs, buttocks and back.

The patient was given 0.2 Gm. of bismuth subsalicylate intramuscularly once a week for eight weeks. The pruritus decreased, but the lesions grew in size and

number. Oxophenarsine (mapharsen®), 0.05 Gm. intravenously once a week for eight weeks, was next administered, with no resolution of the lesions. The course of bismuth subsalicylate was then repeated.

In July 1949 we began to notice for the first time the appearance of follicular papules around each lesion of the original eruption. During the last two months these follicular lesions have become a very prominent part of the picture and are now generally distributed. Pruritus has been paroxysmal, but the patient has no other complaints and generally has felt well.

The past and family history are noncontributory.

On the extensor surfaces of the arms there are sharply defined dime-sized to quarter-sized confluent, irregular keratotic papules, around which are sprinkled pinhead to 0.5 cm. raised, follicular, keratotic papules, some of which show a keratotic plug in the center. The legs and back show similar changes. There are no mucous membrane lesions or definite alopecia.

The hemogram consisted of 3,440,000 red blood cells, 7,550 white blood cells and hemoglobin 66 per cent. The results of urinalysis were normal except for albumin (1+). The Wassermann and Kline reactions were negative.

A biopsy revealed chronic dermatitis consistent with the picture of lichen planus. A biopsy performed on one of the larger hypertrophic lesions also showed the changes of lichen planus. Finally, a biopsy performed on the more recently appearing follicular papules showed changes of chronic dermatitis with focal hyperkeratosis of the hair follicles.

DISCUSSION

DR. H. J. PARKHURST: I thought that this was not a true case of lichen planus, but it reminded me of a couple of cases of arsenic dermatitis of long standing, which I saw years ago, following courses of neoarsphenamine, and I felt that the possibility of arsenical etiology should be entertained in this case.

DR. J. J. STEWART: As far as we could determine, the patient has had no arsenic except the oxophenarsine given to her in the clinic.

DR. G. A. DE OREO: I think that this disorder is lichen planus. I think that the diagnosis is made more obvious because the patient has some very typical lichen planus lesions on the forearm. If these were not present, there might be more room for question. This disease has been called, among other things, lichen spinulosus and folliculitis decalvans (Little) and lichen planopilaris (Pringle). This case presents lesions which are predominantly follicular. There is no question that lichen planus can be produced by toxic agents. Perhaps it can be provoked by arsenic; in the Service we saw it follow long-continued use of quinacrine.

DR. H. N. COLE: This patient does have typical lesions of lichen planus, but the follicular involvement is very unusual in lichen planus. This condition is a true lichen planus, involving the hair follicles, and a section showed these papules as little spiny projections, a picture characteristic of lichen planopilaris. It is an unusual type of the disease. Sometimes these lesions appear on the scalp and cause destruction of the hairs, with alopecia. Just how this destruction is caused is not entirely understood. Little spoke of the condition as lichen spinulosus.

DR. J. R. DRIVER: There has not been very good response to therapy. Because of the follicular involvement, it might be advisable to administer large doses of vitamin A.

DR. G. W. BINKLEY: This case is atypical in the remarkable involvement of the hair follicles, the absence of hyperpigmentation and the lack of response to therpay. I think it is possible that we are dealing with lichen planus here of an etiology different from that of the ordinary type.

Behcet's Syndrome. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

F. H., a Negro woman aged 50, was first seen by us in August 1949, complaining of a "sore" left eye and mouth of three weeks' duration. The disorder began as a slight ulceration of the gum and then spread to involve the inner aspects of the lips, the buccal mucosa, the palate and the tongue, with accompanying hoarseness and fever. The patient received sodium salicylate, to which she became toxic, and penicillin, both intramuscularly and as an ointment applied to the eye, and in four weeks she expereinced improvement but was not entirely free of lesions. Three weeks ago the other eye became red, new ulcers developed in the mouth and the patient complained of "sores" on her genitalia.

She has pronounced conjunctivitis in the right tye, with exudation. On the inner aspect of the upper lip there is an oval superficial ulceration. The buccal mucosa and palate are similarly involved. Inspection of the larynx reveals redness and ulceration of the vocal cords, with ulcerations in the hypopharynx also. Around the urethral meatus there are superficial ulcerations.

Throat cultures showed normal flora and Hemophilus hemolyticus. Smears from lesions in the mouth were negative for diphtheria and Vincent's organisms. Cultures from the conjunctivas repeatedly showed no growths. Blood cultures were repeatedly negative. The results of the Frei and Ducrey tests were negative. No sickle cells were found.

A biopsy was performed on a lesion of the buccal mucosa and revealed acute and chronic inflammation of the mucous membrane, with ulceration.

DISCUSSION

DR. H. N. COLE: I think this case comes closer to being one of Behcet's syndrome than any others I have seen with that diagnosis. In view of a recent report that has appeared on the use of aureomycin for this condition, we are going to give the patient a course of such medication.

DR. C. L. CUMMER: This case does seem to fit in very closely with those presented at the last meeting of the Academy. These eye lesions are frequently terrifically destructive.

Lymphangioma of Hard Palate. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

D. S., a white woman aged 26, states that nearly fifteen years ago she noticed a soft cauliflower-like mass on her gum and several red spots on the "roof" of her mouth. She was never bothered by this lesion and never received any treatment for this condition.

The family and past history are noncontributory.

On the posterior aspect of the left gingival ridge there is a pale, slightly reddish cauliflower-like lesion. Just opposite the gum margin, in the buccal mucosa, there is a similar lesion. Extending from the gingival margin on the left up onto the soft palate there are boggy petechial hemorrhages.

The Wassermann and Kline reactions were negative. The hemogram and results of urinalysis were normal. The platelet count was 130,000 per cubic millimeter of blood, and the bleeding and clotting time, 8 and 2 minutes, respectively.

A biopsy performed on the lesion of the gum revealed irregular spaces lined by flat cells and a narrow rim of collagenous tissue. The stratified squamous epithelium around these spaces showed pronounced intracellular edema.

On April 12, 1949, three 1½ millicurie radon seeds were implanted in the lesion on the left posterior gingival margin. The lesion has regressed about one third of its original size.

DISCUSSION

DR. J. R. DRIVER: Three radon seeds, 1 to each cubic centimeter of tissue, were inserted into the lesion. I would say that it has regressed at least three-fourths its original size.

Steatocystoma Multiplex. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

H. V., a Negro woman aged 25, noticed the appearance of small, nontender "lumps" on the forearms, chest and back three years ago. Since that time they have increased in number, and some in size. She has received no treatment for this condition. They now involve the chest wall also.

When one incises a lesion, a yellowish, odorless, oily liquid exudes. Attempts at staining the oily material failed.

A biopsy performed on one of the nodules revealed a sebaceous cyst.

DISCUSSION

DR. J. R. DRIVER: The nodes are oily rather than cheesy, and I believe that Ormsby states that the oily character is characteristic of this particular condition.

Multiple Basal Cell Epitheliomas Originating from Trichoepithelioma (Epithelioma Adenoides Cysticum); Fibrosarcoma of the Right Mandible; Metastases to the Lung and Lumbar Vertebrae; Leukemoid Reaction Due to Metastasis. Presented by DR. G. W. BINKLEY, DR. H. H. JOHNSON and DR. U. W. LEAVELL (service of DR. H. N. COLE and DR. J. R. DRIVER). (To be reported in detail in a later issue of the ARCHIVES.)

Dermatitis Herpetiformis (Pemphigus?). Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

Acanthosis Nigricans, Juvenile Type? Dermatitis Vegetans? Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

Erythema Annulare Centrifugum; Erythema Gyratum Perstans. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

A Case for Diagnosis: Possible Nevus? Presented by DR. ALLEN E. WALKER.

A Case for Diagnosis: Unusual Melanosis Following Lichen Planus. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

Hydroa Vacciniforme (Hydroa Aestivale) Acquired at Age 30. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

Poikiloderma Vasculare Atrophicans: Squamous Cell Epithelioma with Metastases. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Robert A. Stewart, M.D., *President*

Rees B. Rees, M.D., *Secretary-Treasurer*

Sept. 30, 1949

Familial Benign Pemphigus. Presented by DR. MERLIN T-R. MAYNARD.

V. C., a 28 year old housewife, was seen Aug. 2, 1949, complaining of an eruption over the shoulders intermittently appearing for two years. The lesion seemed to start with light frictional damage, forming thin-walled vesicles which ruptured almost immediately and slowly spread peripherally. Her mother, as well as a maternal uncle, has a similar condition. The mother was seen by me about fifteen

years ago without a definite diagnosis, the condition involving the shoulders but in milder form than is now seen in the daughter. V. C. has been given calciferol and showed no improvement at the end of six weeks. She was given vitamin A ten days ago. Results of blood and urine examinations were noncontributory.

DISCUSSION

DR. GEORGE KULCHAR: I saw 1 person with this condition who showed a dramatic response after three days of aureomycin therapy.

Darier's Disease. Presented by DR. REES B. REES and (by invitation) DR. EDWIN M. HAMLIN.

M. M., a 27 year old student, was well until August 1944. While he was serving in the Army in the South Pacific area, tiny papules appeared on his forehead and back. The lesions were relatively asymptomatic. The course has been one of remissions and exacerbations, with the latter taking place in old areas of involvement or new areas. At various times the scalp, forehead, temples, bearded area and shoulders have been involved. Scattered lesions have appeared on the dorsal surfaces of the hands and feet. There is no familial history of dermatitis, nor is there any known consanguinity.

The lesions are pinhead-sized and larger papules. For the most part they appear to be follicular. They are skin-colored to reddish brown and, except the lesions on the hands and feet, are capped with a dirty brown scale or crust. The lesions which have recently appeared on the left supraclavicular area are surrounded by inflammatory haloes. A tendency to grouping in large patches is noted, especially on the back. Those areas most extensively involved give a hyperpigmented appearance in contrast to that of the surrounding uninvolved skin. We have noted no lesions on the palms or soles or any nail involvement.

Histologic examination showed the characteristic microscopic changes of Darier's disease: i. e., lacunas, corps ronds and grains.

From 1944 to 1948 the patient received various types of local applications, a "full course" of roentgen ray therapy to the face, and desensitization injections for house dust. While he was in the South Pacific area it was felt that the heat aggravated the condition, and he was moved to a cooler climate, but neither this nor any of the aforementioned procedures alleviated the condition. The past year he has been using a mildly peeling lotion and has been taking 150,000 units of vitamin A (not water dispersible) daily. He has also received 325 r to his back Remissions and exacerbations have taken place under this therapeutic regimen, which situation may possibly be explained by the fact that the patient is an ardent sun bather and the sun may have an aggravating influence.

DISCUSSION

DR. MERLIN T-R. MAYNARD: I agree with the diagnosis.

DR. EDWIN M. HAMLIN (by invitation): This patient has had 150,000 units of vitamin A orally daily for the past year. There has been no alteration in the course of spontaneous flaring and subsidence of the lesions. We have the impression that the condition gets worse when the patient is exposed to sunlight.

Scleroderma (Morphea). Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. W. J. COLE.

J. S., a Negro aged 44 years, presented himself at the Stanford University Hospital Dermatology Clinic on Sept. 7, 1949, complaining of "white spots" on

his skin. He stated that in 1946 a small pea-sized papule appeared on the ala of his nose; this subsequently regressed and was followed by an area of depigmentation in the skin. New areas of depigmentation appeared progressively over the nose, right shoulder, sternum and interscapular region.

Examination reveals symmetric discrete to confluent groups of round depigmented areas fading from white centrally to normal pigmentation peripherally, well demarcated from the surrounding normal epidermis and exhibiting a minimal degree of atrophy. Histologic examination of a section of epidermis removed from the region of the right shoulder and from the interscapular region revealed changes compatible with a diagnosis of scleroderma.

Acrosclerosis. Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. W. J. COLE.

A. S., a white man aged 39 years, in September 1946 noticed dull red 3 mm. lesions over the volar aspects of his palms. The reaction to a serologic test for syphilis was positive, and he received arsenobismuth therapy followed by treatment with penicillin. In December 1946 his present complaints appeared, consisting of stiffness in his muscles which appeared first in his hands and then spread to involve the arms, shoulders, abdominal muscles, thighs and lower parts of the legs. Shortly after, he noticed that the skin covering his fingers and toes was tight, stiff, shiny and discolored. For years he had noticed that exposure of his hands to cold temperatures brought about blanching and numbness. In spite of inconclusive data on histologic examination of the skin, apart from myositis, a clinical diagnosis of scleroderma was established, and the patient returned home. He received various medications including neostigmine (prostigmin®), physostigmine, nicotinic acid and padutin® (an insulin-free extract from the pancreatic gland) without improvement. From 1947 to 1949 there has been little change in his skin condition or muscular complaints, but he has had progressive difficulty in retaining food sufficient for adequate nutrition. He has little or no trouble swallowing, but on completion of eating feels "bloated," has eructations and flatulence and frequently vomits a considerable portion of his ingested food. There is obvious atrophy of the muscles of his extremities. The radial pulses are palpable but decreased on the right side; the dorsalis pedis pulses and posterior tibial pulses are absent bilaterally. The fingers are tapered; the nails are curved, and the skin is shiny, atrophic, inelastic and firmly fastened to the underlying structures. Waxy whiteness with some blotchy reddening involves the pulp pads of the terminal phalanx. The fingers are cold. Movement is slow and greatly limited, and extension and flexion are incomplete. The feet are cold and cyanotic when in the dependent position and blanched when elevated. The toe nails appear poorly nourished. The tips of the toes have a blotchy red appearance and there are small areas of atrophy and scarring on the ends of the terminal phalanges although the patient denies ulceration in these locations at any time. The skin over the remainder of the body is not remarkable.

Roentgen examination of the gastrointestinal tract in July 1949 revealed changes compatible with a diagnosis of scleroderma. Histologic examination of a section of epidermis revealed changes compatible with a diagnosis of acrosclerosis.

Scleroderma (Acrosclerosis): Improvement from Treatment with Priscoline® (2-Benzyl-4, 5-Imidazoline Hydrochloride), 150 Mg. Daily. Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. W. J. COLE.

DISCUSSION OF PRECEDING TWO CASES

DR. GRANT MORROW: In the first case I felt no hardness of the skin. The condition appeared more like a vitiligo to me.

DR. FREREDICK G. NOVY JR.: I thought of leukoderma.

DR. EUGENE FARBER: Clinically the lesions are not indurated, but histologically they are typical of scleroderma. There are fragmentation of the connective tissue and changes in the elastic tissues, for example.

DR. KEMP DOWDY: I saw a case of leukoderma similar to this clinically about three months ago. The lesions were painted with 95 per cent phenol solution with the hope of stimulating melanin production. After one treatment the patient went to sea. When he returned six weeks later most of the lesions showed a return of pigment.

DR. OTTO E. L. SCHMIDT: I thought on inspection that the condition was vitiligo. However, on the slide one can see pronounced sclerosis throughout the entire cutis.

DR. HERMAN ALLINGTON: I suggest the use of vitamin E for a long period. In 1 case of localized scleroderma which I have been following there is slow improvement under this regimen.

Status Dysraphicus (Familial Syringomyelia) with Bilateral Foot Ulcers. Presented (by invitation) by DR. M. F. ALLENDE.

R. P., a 29 year old married white woman, was first reported in the medical literature in 1942 (Mulvey, B. E., and Riely, L. A.: *Ann. Int. Med.* **16**:966-994, 1942) as a member of a family group afflicted with status dysraphicus. She was first seen at the University of California Hospital on Aug. 12, 1949.

When she was first brought for study in 1948 because of her family association, it was found that she had had excessive sweating of her feet all her life and that she had sustained several painless minor injuries to her feet. For the last nine years she has had recurrent ulcers of both soles following burns and injuries. At times necrotic bone would be found in the dressings. For the last two years the ulcers have been almost continuous and secondary infection has been controlled by frequent injections of penicillin. In addition to other members of the family, 4 of her 6 siblings present similar disturbances.

Physical findings were normal, except for the following (Aug. 12, 1949): There is a 1.5 by 1.5 cm. round area of granulation tissue, elevated 0.5 cm. above skin level on the ball of the right foot, and a 1 by 2 cm. ulcer with a deep crater on the left foot. There is absence of the dorsalis pedis pulsation on both sides and absence of pain and temperature sensations of both feet and ankles. Roentgen examination showed areas of rarefaction of the first metatarsal bone and proximal phalanx of the great toe on both sides.

DISCUSSION

DR. FRANCES A. TORREY: This is an interesting familial type of syringomyelia. It apparently is due to gliosis of the neural tube. In 500 cases taken some 18 showed slight changes which represented syringomyelia. There may be all grades of this particular entity.

A Case for Diagnosis. Presented by DR. HERBERT LAWRENCE.

D. F., a 28 year old woman, has a psoriasiform eruption which started on the feet late in 1947. During the succeeding year the lesions ascended to the legs and

gradually involved the trunk and arms. Characteristically the lesions diminish and increase in severity. However, some evidence of the eruption has been continuously present since the onset. Pruritus varies from minimal to severe. The onset of the eruption coincided with an emotional breakdown associated with alcoholism. There is a history of infantile eczema present until the age of 5. Obesity was first evident at the age of 20, at which time the patient's weight went from an average of 150 pounds (68 Kg.) to over 200 pounds (91 Kg.). Biopsy from a lesion of the foot was not of diagnostic significance.

DISCUSSION

DR. GEORGE KULCHAR: I suggest parapsoriasis en plaques.

DR. FREDERICK G. NOVY JR.: Why not guttate psoriasis?

DR. GEORGE KULCHAR: I believe it is a mixed type with predominantly the en plaques variety.

DR. EDWARD RINGROSE: Clinically the disorder is suggestive of secondary syphilis.

DR. HERBERT LAWRENCE: Parapsoriasis was considered, but since it is primarily a descriptive diagnosis further understanding of the case was sought. In the June 1949 issue of the *Pennsylvania Medical Journal*, Dr. Helen Drant reported 100 dermatologic cases associated with endocrine disease. Ten cases were described in detail with photographs. One in particular fits the clinical picture of my patient. In both Dr. Drant's cases and mine there were hypogonadism, hyperthyroidism and obesity. My patient is being studied by an endocrinologist.

A Case for Diagnosis: Lichen Planus, Aberrant Type? Presented by DR. EUGEN OSTWALD.

C. P., a 58 year old Mexican housewife, a resident of San Francisco for more than thirty years, noticed in September 1948 dark brownish discolorations on her neck, under both breasts and in both armpits. She believes that she first noticed a slight stinging sensation of her arms; otherwise there were no subjective skin symptoms. Except compound effervescent powders as a laxative, there has been no drug intake. When we first saw the patient, on Feb. 8, 1949, there was an almost uniform deep black-brown pigmentation, most pronounced around the neck, at the flexor surfaces of both arms, underneath both breasts and extending far down on the abdomen to the inguinal regions and thighs. The follicles, particularly of the trunk, breast, abdomen and arms, showed a distinctive keratotic involvement. Results of glucose tolerance tests were normal, and the results of examination for uroporphyrin were negative. The basal metabolism rate was — 17 per cent. A biopsy was taken March 7, 1949. Dr. Gerson Biskind reported that the skin was covered by a relatively thin epidermis which showed a moderate degree of keratosis and follicular plugging. The epidermis showed very few distinct rete pegs. There was a scattering of mononuclear and polymorphonuclear leukocytes in the epidermis, as well as in the underlying corium. The infiltrate in the corium was limited mainly to the upper third. There were many pigment-containing macrophages in the corium associated with the inflammatory infiltrate. A scant bit of pigment could be found in some of the epithelial cells, in which it was present as very fine granules and seemed to be situated between the cells. An occasional macrophage containing pigment also was seen to have penetrated the epidermis. The cells of the corium were mainly leukocytes and slightly larger macrophages. There were no distinct plasma cells. Iron stains showed that the

pigment was melanin. The microscopic diagnosis was that the skin showed slight atrophy of the epidermis, with hyperkeratosis and follicular plugging, and melanin deposit and lymphocytic infiltrate in the corium.

The clinical picture has changed recently. The deep, uniform pigmentation has changed into a netlike appearance around the neck and has practically disappeared underneath both breasts and at the axillas. The arms now show reticular lichen-like lesions. Treatment has consisted of the administration of bismuth subsalicylate intramuscularly, vitamins A and B orally and the application of 2 per cent salicylic acid ointment locally.

DISCUSSION

DR. FRANCES A. TORREY: Dr. Hiram Miller in 1945 reported a case of lichen verrucosus et reticularis which clinically resembled this. Tonight there is a pronounced regression in the lesions.

DR. REES B. REES: I do not believe this condition is lichen verrucosus et reticularis because there is not the pronounced verrucous element and because there has been improvement in the lesions. The original case reported by Kaposi and later on by Nekam showed lesions on the face which were reminiscent of lupus erythematosus or seborrheic dermatitis, as well as conical papules on the buttocks. There was a striking reticulated pattern with a tremendous verrucous element capped by scale in the original case.

DR. CHARLES MCNITT: This patient has complained of itching, which would be compatible with lichen planus.

DR. MERLIN T-R. MAYNARD: Does this patient have mucous membrane lesions? In a case that I saw there was involvement of the anal membrane. I believe anal involvement has not been reported.

DR. EUGEN OSTWALD: Except for pigmentary discolorations, neither oral nor vaginal mucous membrane lesions could be noticed. The striking change in the clinical picture, particularly of the smooth dark pigmentations beneath both breasts, which have shown complete involution, is a point of special interest. The pronounced, deep, uniform, smooth pigmentation of large body areas is reminiscent of cases of melanosis seen in Germany after the first world war. The lesions of both arms, as they are now, suggest very strongly lichen planus. However, I believe the widely distributed follicular keratosis is very unusual.

A Case for Diagnosis: Dermatitis Colonica? Presented by DR. EDWARD J. RINGROSE.

G. S. M., a 41 year old white man, has been troubled with a recurrent skin eruption since 1945, when he was in the United States Army in Germany. This has been an eczematoid dermatitis of variable severity, involving chiefly the feet and lower extremities. For the past year he has had a recurrent eruption of the axillas, arms, thighs, buttocks and abdomen. There has been only slight itching. In the axillas, on the adjacent trunk and arms, on the lower part of the abdomen and on the upper portions of the thighs there are multiple erythematous, scaling maculopapules varying in size from a few millimeters to 3 cm. Some of these show clearing in the center and a bright erythematous border. The results of physical examination were entirely normal. The hemogram and results of urinalysis have been repeatedly within normal limits. The reaction to the trichophytin skin test was negative. Multiple scrapings for fungi were negative. Treatment has included penicillin therapy, many local applications and elimination of possible foci of infection in tonsils and prostate, all without avail. In addition, ultraviolet irradiation and roentgen ray and foreign protein therapy have been without benefit.

DISCUSSION

DR. HARRY ALDERSON: What is dermatitis colonica?

DR. EDWARD RINGROSE: It is an eruption which resembles pityriasis rosea or parapsoriasis en plaque. Whitfield described the first case in which there was a relative lack of the colon bacillus in the bowel with an increase in streptococci.

DR. REES B. REES: I believe this is a dermatophytid in spite of the fact that repeated examinations for fungous involvement of the feet have failed to reveal any. Furthermore, the reaction to the trichophytin skin test with a dilution of 1:30 was negative.

DR. EDWARD RINGROSE: I thought of dermatophytid also. All scrapings were negative.

DR. KEMP DOWDY: I agree with the diagnosis of dermatophytid. This is a pityriasis-rosea-like id eruption.

Coccidioidal Granuloma. Presented by DR. EDWARD J. RINGROSE and (by invitation) DR. G. H. EKBLAD.

A 25 year old white man, a lifetime resident of Fresno, Calif., except for some time in the Service, first noticed weakness and chest pains in June 1949. Small "pimples" appeared on his skin two months later. He now has multiple asymmetric granulomatous lesions of lentil to split pea size on his face, neck, trunk and sacrum. Microspherules with endospores were demonstrated on direct smear from a lesion on the chin. The patient was found to have a mild secondary anemia. The leukocyte count was normal except for a 34 per cent eosinophil count. The reaction to the Kahn test was negative. The coccidioidin reaction was negative in a 1:100 and a 1:10 dilution on Sept. 8, 1949. The temperature ranged from 98 to 102 F.

Histopathologic examination showed ulceration of the epidermis with granulomatous tissue beneath it. There were numerous epithelioid cells, as well as small round cells, plasma cells and eosinophils. A few scattered giant cells were found, and a careful search showed only 3 rounded double refractile bodies measuring from 22 to 26 microns. These structures were typical of Coccidioides immitis. One of the spherules contained endospores. The diagnosis was coccidioidomycosis of the skin.

DISCUSSION

DR. GRANT MORROW: How would you treat this condition?

DR. EDWARD J. RINGROSE: In June 1948 I presented a similar case in which the patient had been treated for a few months with coccidioidin without benefit. The local granulomatous lesions were then treated with radiation from an aerokromayer lamp with a good response. However, this may have been a spontaneous remission.

DR. FRANCES A. TORREY: We presented a case here a year ago, of a 35 year old man with multiple lesions of his face and back all of which cleared except one on the back. The patient has had no special treatment.

DR. ROBERT LOFGREN: The presence of facial granulomas is said to give a poor prognosis, with the possibility of a fatal outcome.

DR. EDWARD RINGROSE: Some of the patients do recover.

DR. ERVIN EPSTEIN: The prognosis in coccidioidal granuloma is not dependent on the location of the lesions as much as on the type of lesion. The lesions of miliary coccidioidal granuloma are mulberry-like and are often confused with an ioderma, bromoderma or multiple granuloma pyogenicum. At the Oakland

Veterans' Hospital there have been 5 cases with fatal outcomes, death being due to miliary coccidioidal granuloma. Three of the patients presented the aforementioned fungating type of cutaneous lesions. I do not believe that the prognosis in the present case is very bad.

Early Indeterminate Leprosy. Presented by DR. EDWARD J. RINGROSE and (by invitation) DR. G. H. EKBLAD.

A 26 year old Filipino man first noticed scattered macules and slightly raised ovoid lesions up to 1 cm. in diameter in March 1949. He had slight nontender bilateral epitrochlear adenopathy at that time. He was on sea duty until the end of July 1949. He has remained free of symptoms and fever. There has been very little change in the preexisting lesions, but a few new ones have appeared. He lived in the Philippines all his life until joining the Navy three years ago. He knows of no contact with leprosy. There are fairly symmetrically distributed rounded, oval, slightly erythematous macules and maculopapular lesions over the arms, face, neck, trunk and legs. These are from 2 to 10 mm. in diameter. The patient has a contact dermatitis of his right arm and shoulder from nitromersol (metaphen®) or elastoplast® applied at the site of a biopsy. In addition to the skin changes he was found to have hypesthesia of the ulnar surfaces of both elbows. There was also generalized shotty adenopathy. A smear from a gland biopsy specimen was positive for Mycobacterium leprae. Results in the Kahn test, urinalysis and complete blood test were normal.

The lymph node biopsy specimen taken on Sept. 28, 1949, showed many packets of acid-fast bacilli characteristic of the causative organism of leprosy. The histologic section showed normal architecture except for an infiltrate composed largely of epithelioid cells and lymphocytes.

There has been no treatment.

DISCUSSION

DR. PAUL FASAL: Have a lepromin test and a determination of the sedimentation rate been performed?

DR. EDWARD J. RINGROSE: We do not have lepromin available.

DR. PAUL FASAL: It is not absolutely necessary to wait three weeks until the result of a lepromin test can be read, as originally suggested by Mitsuda. According to Fernández, lepromin tests can be read also after forty-eight hours and in most instances the reading after forty-eight hours is identical with the reading after three weeks. I shall be glad to provide the lepromin. I feel that this case is of lepromatous leprosy and not of indeterminate leprosy. I suggest that you determine the sedimentation rate as that procedure also helps in the differentiation of the types.

DR. EDWARD RINGROSE: The pathologic examination indicates that the disorder is probably of the lepromatous type.

Lymphangioma Circumscriptum of the Tongue. Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. W. J. COLE.

H. Z., a 34 year old white man, was admitted to the Stanford University Hospital Dermatology Clinic on May 18, 1949. He dates the onset of his trouble from the age of 2 years, when he fell and traumatized his tongue. From that time on, approximately two times yearly, his tongue enlarges and becomes stiff, tender and rough. The entire surface of the tongue is involved by small cystic lesions; some are clear, some of a yellow hue and some decidedly hemorrhagic and purplish. They vary from 1 to 3 mm. in diameter.

Histologic examination shows large endothelium-lined vascular channels in the submucosa. One measures nearly 0.5 mm. in diameter and has a large clump of lymphocytes in the lumen. The predominant change, however, is hypertrophy of the surface epithelium with papillary projections into the submucosa.

The members of the Tumor Conference, Stanford University Hospital, advised against local roentgen therapy as this type of lesion is extremely radioresistant.

Multiple Benign Tumor-like New Growths of the Skin (Schweninger-Buzzi). Presented by DR. FRANCES A. TORREY.

R. C., a 36 year old man, had primary syphilis in 1935. No history of secondary lesions was obtainable. He was treated in 1941, presumably with heavy metals, and in 1948, with penicillin. Four years ago he noted atrophic spots on his trunk and upper extremities with a gradual increase in number but without symptoms. He has a duodenal ulcer and early rheumatoid arthritis, both of recent onset. Reactions to serologic tests for syphilis were negative. The amount of hemoglobin, the white blood cell count and results of urinalysis were normal. There are oval, atrophic lesions on the upper part of the trunk and proximal extremities. The skin over the lesions has an "orange peel" appearance; on palpation lack of resistance in the corium is noted, and the epidermis can be invaginated through the surrounding ring.

Slides with hematoxylin and eosin and Weigert stains are presented.

DISCUSSION

DR. WILLARD MEININGER: I favor a diagnosis of syphilitic macular atrophy.

DR. FRANCES TORREY: There is no history of a syphilitic eruption.

A Case for Diagnosis (Sarcoid? Lupus Erythematosus?). Presented by DR. ARNE E. INGELS.

A Case for Diagnosis: Morphea? Pseudopelade? (Cicatricial Alopecia). Presented by DR. EUGENE M. FARBER.

A Case for Diagnosis: Psoriasis? Seborrheic Dermatitis? Neurodermatitis Circumscripta? Lupus Erythematosus? Presented by DR. KEMP DOWDY.

Scleredema Adultorum. Presented by DR. WILLARD M. MEININGER.

Lupus Erythematosus, Subacute? Micropapular Tuberculid? Presented by DR. OTTO E. L. SCHMIDT and (by invitation) DR. W. J. COLE.

Pityriasis Lichenoides and Varioliformis Acuta Haberman (Parapsoriasis Varioliformis) in a Negro Girl. Presented by DR. PAUL FASAL.

Atopic Dermatitis. Presented by DR. MERLIN T-R. MAYNARD.

Tripelennamine (Pyribenzamine®) Dermatitis? Roentgen Reaction with Toxic Eruption? Presented by DR. ERVIN EPSTEIN.

CHICAGO DERMATOLOGICAL SOCIETY

Carl W. Laymon, M.D., *President*
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Oct. 19, 1949

Nodular Vasculitis. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. D. COHEN and DR. S. BARSKY.

DISCUSSION

DR. M. J. REUTER, Milwaukee: In the past most of us diagnosed these nodular lesions on the lower extremity as erythema induratum of tuberculous etiology. We are indebted to Drs. Montgomery and O'Leary for pointing out

that these nodular lesions with or without ulcerations may be nontuberculous as well as tuberculous. Many of these persistent nodular lesions on the lower extremities, especially those in elderly women, are nontuberculous, and the term nodular vasculitis seems apt as it does describe the histopathologic changes although the cause remains obscure.

DR. H. E. MICHELSON, Minneapolis: I should like to know just what the term nodular vasculitis means. Is the disorder an acute condition? Is it a chronic condition? Is it recurrent? Is it connected with the veins? Is it the result of thrombophlebitis? Just what is it? I have seen cellulitis called nodular vasculitis. I have seen chronic sclerodermic infiltrate resulting from chronic thrombophlebitis also called nodular vasculitis. The term nodular vasculitis is used as a label for erythema-induratum-like lesions that cannot be classified as tuberculous. The microscopic picture of inflammation of the fatty tissues is surprisingly similar in many instances, and therefore the histologic features alone do not give a basis for differential diagnosis. I believe we need a much clearer definition and sharper recognition of boundaries when we discuss these conditions.

DR. CARL W. LAYMON, Minneapolis: At the last meeting of the Minnesota Dermatologic Society in Rochester Dr. O'Leary said that a diagnosis of nodular vasculitis was made after the possibility of other disorders, such as phlebitis migrans and erythema induratum, had been excluded.

DR. THEODORE CORNBLEET: I can understand Dr. Michelson's dissatisfaction with the term nodular vasculitis, since it merely characterizes something anatomically without committing itself as to etiology. This name, however, rolls off the tongue easily and is reasonably descriptive. It is suspected that more than one cause for these nodose lesions must be present in the subjects with them, and when these underlying factors become known suitable adjectives characterizing them can be added to the anatomic stem.

Sarcoidosis. Presented by DR. D. OMENS and (by invitation) DR. H. OMENS and DR. D. MUSGRAVE.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I am glad that Dr. Riehl is here to give us his views on sarcoidosis. All of us who are interested in this subject must of necessity change our point of view from time to time for there has been nothing very definitely new in the past year. Those who specialize in diseases of the chest are paying much more attention to sarcoidosis, and they are inclined to classify the lung condition with the fibroses of the lung, but I am sure that many lesions of the lung are absorbed without fibrosis. The percentage of error in the diagnosis of sarcoidosis varies greatly in each specialty. I believe we dermatologists have the highest percentage of accuracy because we have the advantage of observing both the clinical and the microscopic picture. For the chest, the roentgenologists are very wary about making a positive diagnosis. The roentgenograms of the bones, on the other hand, offer very accurate information. In the case presented the history sheet stated that the patient had osteoarthritis. This observation is most unusual because there is rarely arthritis reported in patients with sarcoidosis.

DR. GUSTAV RIEHL, Vienna, Austria (by invitation): In Austria we see very little sarcoidosis, especially of the dystrophic type. What we see is the pernio type. In many cases we see pulmonary changes going along with the bone changes, with cystic formation and so on. We would not make a diagnosis from the changes in the lung alone. I have never seen sarcoidosis of the dystrophic type

with osteoarthritis. Pautrier in Paris claimed that Schaumann's disease was not tuberculosis. He stated that he had had no experience with the use of vitamin D in the treatment of this disease, but our experience with it is favorable. My associates and I found out that pernio responds to vitamin D much later than does lupus, and we think this might be an indication that certain cases of sarcoidosis are of tuberculous origin.

Ringed Hair (Pili Annulati) in a Woman Aged 30. Presented by DR. L. E. TAVS.

DISCUSSION

DR. L. E. TAVS: The case was shown only for its academic value. According to the literature, about 50 per cent of the cases have a hereditary factor. Reyn in 1934 reported on 8 cases in four successive generations in the same family. As the history stated, a brother of the present patient has the same condition. Cady and Trotter expressed the belief that the white rings were due to gas in the cortex of the hair shaft, which they thought was carbon dioxide. They were unable to explain how the gas got there. They added 5 per cent sodium hydroxide to these hairs, and the rings disappeared. We tried that treatment, and the rings disappeared as we watched them in two or three minutes.

A Case for Diagnosis. Presented by DR. E. M. SMITH.

Mrs. W. C. D., a white housewife aged 46, was first seen on Aug. 27, 1949, with a symmetric eruption on the inner side of her legs which had started in June. The lesions were flat with a scaly surface and a slightly raised margin; the clearing in the center was accompanied with a brownish green pigmentation. The lesions were roughly kidney shaped.

Since that time the areas have enlarged considerably and new areas have developed on the body. There are no subjective complaints.

In laboratory examinations the Kahn and Wassermann reactions were negative; the red blood cell count was 4,210,000; the white blood cell count, 10,250; hemoglobin, 78 per cent, and the blood platelet count, 404,160.

A biopsy specimen from the edge of one of the lesions was reported as chronic dermatitis of undetermined type, showing mild hyperkeratosis and parakeratosis with a lymphocytic infiltrate of the superficial portion of the dermis, together with edema of the collagen fibers.

DISCUSSION

DR. ASHTON L. WELSH, Cinncinnati: I do not know that I can make a positive diagnosis. I was disappointed when I saw the section. Because of the lack of changes observed in the section, I thought the disorder might be grouped as xanthoerythroderma perstans. I could not learn from the patient today whether she had had any drugs.

DR. STEPHEN ROTHMAN: Was tinea circinata excluded?

DR. E. M. SMITH JR.: No examinations were made.

DR. STEPHEN ROTHMAN: The lesions display more scaling on the border than in the center. Such an "active border" would be rather unusual for parapsoriasis en plaques.

DR. J. F. MADDEN, St. Paul, Minn.: I think that the patient has psoriasis. I have been using undecylenic acid in the treatment of psoriasis for several months. The eruption has not involuted in any of the 70 cases in which undecylenic acid has been used. The condition of 4 persons with psoriasis with few lesions progressed

to generalized exfoliative dermatitis while undecylenic acid was taken. One patient acquired auricular fibrillation after taking undecylenic acid for two months. Treatment with the drug was discontinued, and the auricular fibrillation ceased after two weeks. Because of my observations to date, I think that undecylenic acid is of little or no value in the treatment of psoriasis and that it should not be given indiscriminately in large amounts because of the ill effects observed in my cases.

DR. M. R. CARO: I should like to agree with the diagnosis of psoriasis clinically. The section showed so few pathologic changes as compared to the lesion itself that I think it may have been taken from a lesion undergoing resolution. I would suggest that another biopsy be taken from an active lesion.

DR. CLARK W. FINNERUD: I considered parapsoriasis. The nail of the left ring finger had a single pit in it similar to the sort seen in psoriasis. At the very left hand borders of the section there were changes compatible with those of psoriasis, though one could hardly make such a diagnosis from the observations in the section alone. I should not be surprised if this condition proves to be psoriasis.

DR. ASHTON L. WELSH, Cincinnati: The reason for the diagnosis of xantho-erythoderma perstans was that the lesions that are receding, particularly the large plaque on the right calf, show destruction or atrophy. They become yellowish or bronze. I would be grateful if Dr. Smith could get a biopsy from the center of that large receding plaque.

Urticaria Pigmentosa of Fifteen Years' Duration in a Woman Aged 41.
Presented by DR. JAMES H. MITCHELL and DR. M. H. EBERT.

Tissue fixed in 3 per cent lead acetate and stained with toluidine blue showed mast cells with large oval nuclei, and numerous purple-staining metachromatic granules in the cytoplasm were most numerous about the papillary and subpapillary vessels. Long dendritic projections of the cytoplasm contained the metachromatic granules.

In a section fixed in absolute alcohol stained with hematoxylin and eosin the mast cells were recognizable by the large oval nuclei with fine, relatively light-staining chromatin. The cytoplasm and granules were not visualized. In places these nuclei were clumped to form giant cells.

Normal skin from the back fixed in 10 per cent basic lead acetate and stained with toluidine blue showed a moderate number of mast cells in the walls of the subpapillary vessels, with metachromatic purple granules in the cytoplasm. These features were also present in the walls of the deeper vessels of the corium.

DISCUSSION

DR. NORMAN TOBIAS, St. Louis: I thought it was very interesting to see a case of this type occurring at this patient's age. The patient did not complain of much itching. The dull red color which disappeared on diascopic pressure, leaving a slight brownish pigmentation, is not a feature of the common type of urticaria pigmentosa as seen in adults. I would classify this case as an example of telangiectasia macularis eruptiva perstans.

Dr. M. H. EBERT: This case was shown particularly on account of the method of staining the granules in the mast cells. In the last few years there has been renewed interest in mast cells due to the work of Jorpes and his associates in Sweden. They expressed the belief that the granules in mast cells are heparin and are a very powerful anticoagulant. For years it has been pointed out that mast cells have some function. They are found in normal skin. A section of normal

skin fixed with basic lead acetate and stained with toluidine blue which was presented today showed a goodly number of mast cells. The reason the tissue is fixed in basic lead acetate is that heparin is water soluble and diffuses out in ordinary methods of fixation. Some of the anatomists have gone so far as to call mast cells unicellular glands. Jorpes stated the belief that that is what they are. They have some function. They are found in large numbers near the joints, in the eye and in places where considerable hemorrhage may occur without clotting. Jorpes' interest in this problem was aroused by the work of a Belgian anatomist by the name of Lisson, who showed that metachromatic staining with toluidine blue is due to the presence of sulfuric acid esters of polysaccharides. By some ingenious experimental methods Jorpes and his group in Sweden demonstrated that in whatever tissue one finds large numbers of mast cells one can extract a considerable amount of an anticoagulant, which they assumed to be heparin. When the tissues contain little or no mast cells no anticoagulant can be extracted. Since heparin is a sulfuric acid ester of mucoitin Jorpes and co-workers concluded that the metachromatism of the heparin granules is due to its structure. In urticaria pigmentosa there seems to be an abnormal development of mast cells far beyond the number ordinarily present about the small blood vessels. It has been impossible so far to demonstrate any physiologic effect of this excess of heparin on the coagulating power of the patient's blood.

Another interesting point is that these lesions urticate—that is, they wheal—which would indicate the presence of histamine. Thus the lesion of urticaria pigmentosa contains heparin and when stimulated can produce histamine. Both these substances are found in certain forms of anaphylactic shock, in the dog, for instance. Their presence in these lesions may have some bearing on the allergic phenomenon.

A Case for Diagnosis. Presented by DR. F. E. SENEAR and STAFF.

R. S., a 21 year old white man, was seen in the Department of Dermatology, University of Illinois Research and Educational Hospital, on Sept. 15, 1949, because of a generalized skin eruption of nearly lifetime duration. At 6 weeks of age he first had an eruption on the face, buttocks and extremities, which recurred until he was 5 years of age, when a chronic, weeping dermatitis appeared on the lower extremities. The original lesions were said to have been blisters appearing at sites of trauma. The eyesight became progressively diminished, and the right eye was enucleated on Aug. 10, 1934, because of a "chronically inflamed and hopelessly blind eye." A diagnosis of bilateral symblepharon was made then. Subsequently some "blisters" developed about the finger and toe nails, with progressive loss of the nail plates. Visual perception in the left eye decreased, and the conjunctiva gradually became constricted, with shrinking of the left eyelids. The skin of the face and neck became dry and flushed, and many lentigines developed. Treatment was of little benefit until one year ago, when streptomycin was given for three months, with clearing of the weeping eruption on the legs and disappearance of the "blisters" about the nails. The parents are second cousins. The father died of cancer of the skin of the feet and legs and had skin changes similar to those exhibited by the patient. There are three sisters and one brother with no history of skin disease.

Physical examination reveals a thin white man with dry, atrophic, erythematous skin of the face and sides of the neck, with many lentigines and some telangiectasia. The right eye is missing, and there is almost complete loss of the left eyelids, with conjunctival shrinkage. On the legs there are bluish, atrophic, dry and slightly scaly sharply marginated areas of dermatitis. There is pronounced atrophy of toe and finger nails.

DISCUSSION

DR. HOWARD J. PARKHURST, Toledo, O.: Most of these lesions and resulting scars are located on sites of trauma. I thought this case might be one of epidermolysis bullosa.

DR. STEPHEN ROTHMAN: In very severe cases of the destructive form of epidermolysis bullosa we do see these widespread extremely severe atrophic changes. Loss of vision is by no means uncommon. When the patient was questioned he distinctly stated that although he does not get bullae from pressure he does get them from slight injury. It would be of interest to know whether the patient has porphyria.

DR. HAROLD SHELLOW: The preponderance of the eruption on the exposed parts of the body and face and upper extremities led me to believe that we might be dealing with some disturbance of porphyrin metabolism.

DR. FRANCIS E. SENEAR: We felt that a great deal of this picture was concerned with a very severe destructive form of epidermolysis bullosa. On the other hand, with the history of superficial cancer in the father and the changes seen here, xeroderma pigmentosum would have to be considered. I have never seen, as Dr. Rothman said, any cases of epidermolysis bullosa so extensive as to give rise to changes like these. In casting about for some other diagnosis we covered the situation by saying the condition was some unusual type of congenital disturbance.

Beryllium Granuloma. Presented by DR. OLIVER ORMSBY and DR. M. H. EBERT.

K. Z., aged 15, cut his right index finger two months before his admission while breaking a fluorescent light bulb. The wound healed uneventfully, but shortly afterward a tumor, which has increased in size, developed in this area. When first seen by us the patient presented a raised dome-shaped bluish red nodule 1.5 by 2 cm. The tumor was moderately firm. The epidermis was normal except for the scar.

The tumor was removed by Dr. John Dorsey at the Presbyterian Hospital, and photomicrographs of sections from the tumor are presented. The structure resembles very closely that of a sarcoid nodule with the exception that in the upper part of the nodule there is a tendency for the nests of epithelioid cells to fuse and break down. Results of animal inoculations were negative. No acid-fast bacilli were demonstrated. No bacteria of any type were visible. Examination with dark field illumination and with the polariscope revealed no particulate matter.

DISCUSSION

DR. M. H. EBERT: There was no possibility of presenting the patient. He was a healthy boy of 15, and I do not know whether it would be good for his psyche for him to be deluged with questions that might arise in the minds of this group. All the patient presents now is a scar. Several months ago he cut his finger while breaking up a fluorescent light tube. The wound healed, and gradually the tumor began to grow. When Dr. Ormsby and I saw him it was about the size of a half hazelnut and had a bluish coloration. With that history we felt that the tumor was a beryllium granuloma. The lad had already made the diagnosis himself. He said, "Yes, my uncle is in the electrical business, and that disease has been described in the electrical journals, and we felt that that was what it was."

The interesting part is that the sections so closely simulate sarcoid; in other words, the tumor is a localized sarcoid. Dr. Hass, the pathologist at Presby-

terian Hospital, expressed the opinion that there must be particles in the skin to stimulate this growth. He went to some trouble trying to demonstrate minute particles which might stimulate the growth but found none. A spectroscopic examination for the presence of beryllium was not made. This beryllium granuloma is an entirely different disorder from acute and chronic beryllosis, which are systemic disorders. Dr. Hass has expressed very strongly the opinion that this development would not happen in every person. He stated that there are millions of lamps used throughout the country and youngsters that break them but that the cases of beryllium granuloma are very, very few. Consequently, he stated the belief that there is something about the patient as well as about the beryllium that produces such a reaction. Beryllium is extremely active chemically and probably unites with some organic substance in the body to produce the granuloma. When the lesion is removed it should be removed in toto. In this case there is no ulceration, but ordinarily the tumors do ulcerate. Those of you who attend the Academy will hear of the most recent development in this field when Dr. Dutra of Cincinnati presents his paper. It would be interesting to know whether the result of the Quiem test would be positive in this case.

Subacute Lupus Erythematosus. Presented by DR. F. E. SENEAR and STAFF.

J. M., a 21 year old white woman, was seen in the Department of Dermatology, University of Illinois College of Medicine, on Oct. 14, 1949. There was a history of an eruption of the cheek of two and a half years' duration, previously treated by means of injections of a bismuth preparation, administration of vitamin E and applications of solid carbon dioxide. In March 1949, two days after delivery of a normal infant, she had pronounced swelling of the face and extremities, numerous large blisters, falling of the hair, joint pains and swelling and high fever. Symptoms subsided after about one month, leaving the original area on the cheek practically unchanged.

Examination revealed patches of discoid lupus erythematosus on the right malar region and on the left side near the nose. There were areas of superficial ulceration in both lesions. There was a widespread distribution of pigmented, irregularly ringed spots, according to the patient marking the sites of the previously present bullae.

Subacute Lupus Erythematosus in a Man. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. D. COHEN and DR. S. BARSKY.

J. M. is a 46 year old American Indian who first acquired the cutaneous manifestations of disseminated lupus erythematosus in November 1945.

He states that he was completely well until September 1943, when he had generalized joint pains and malaise with progressive loss of weight. Since the onset he has never been completely well although he has had many remissions and exacerbations. He has been afebrile for the past year.

He presents discrete, scaly, irregular, atrophic, hyperpigmented patches confined mostly to the butterfly area of the face, ears, neck and extensor surfaces of the extremities. Some of the lesions are mildly inflammatory. Pernio-like lesions involve the fingers and palms; the toes and soles are also involved but to a lesser degree. The scalp and mucous membranes are free of lesions.

Many of the stigmas of androgen deficiency are evident—youthful appearance, absence of normal male scalp line, high-pitched voice and sparsity of chest hair. A biopsy of testicular tissue revealed atrophic testicular tissue with edematous interstitial connective tissue.

Laboratory observations were as follows: urine—reaction for albumin, 2+; reaction for glucose, negative, and microscopic elements, none; and blood—Kahn reaction, negative; hemoglobin, 89 per cent; polymorphonuclear neutrophils, 72; polymorphonuclear eosinophils, 0; polymorphonuclear basophils, 0; lymphocytes, 24; monocytes, 4; white blood cell count, 5,600; nonprotein nitrogen, 38 mg.; total protein, 8.8 Gm. per cent; albumin and globulin 5.1:3.7 Gm. per cent; glucose (fasting blood) 181 mg., and cholesterol esters, 64 mg. per 100 cc. A roentgenogram of the chest was normal. In a muscle biopsy no pathologic changes were seen in deltoid and pectoral muscles. In a biopsy of the skin features were seen compatible with lupus erythematosus.

DISCUSSION OF PRECEDING TWO CASES

DR. GUSTAV RIEHL, Vienna, Austria (by invitation): The patient in case 1 gave a history of having had a rash a few days after delivery. This point reminds me of a case observed in Vienna in which the opposite occurred. A woman with very acute lupus erythematosus was practically dying. We did what we could, but there was no result from our therapy. When she delivered, the lupus erythematosus began to improve in a few days. Later the patient had a recurrence and died. This account indicates that maybe there is some relation to the endocrine glands in lupus erythematosus acutus. The patient had a strong parallel to what we see in psoriasis. You have all probably seen cases over the years in which psoriasis healed during pregnancy, and others in which the psoriasis accompanied pregnancy. This occurrence might be due to some connection with the adrenal cortex.

DR. H. E. MICHELSON, Minneapolis: My associates and I have used ACTH in a case of hyperacute lupus erythematosus. The patient had a temperature of 105 F., a white blood cell count of 2,300 and all the other expected observations. After the administration of the drug, the temperature dropped to 99 F., the edema left the face and, except for pigmentation, the condition was decidedly improved; however, we had to stop administration of the drug, and the temperature rose, but only to 99.5 F. The drug certainly offers something for the future. I wonder whether anyone else here has had experience with the use of ACTH in this disease.

DR. HERBERT RATTNER: I have observed 2 cases in which ACTH was used. One was of a young girl with a full-blown acute disseminated lupus erythematosus, typical in all respects both clinically and according to laboratory observations. She appeared to be dying despite treatment with antibiotics, vitamin E and para-aminobenzoic acid. The first injection of ACTH produced striking improvement, and improvement progressed to the point where the patient was able to leave the hospital after about three months of treatment. When treatment with ACTH is discontinued, symptoms of joint aches, fever and flush make their appearance, so that it is necessary for the patient to receive ACTH daily.

The other patient had psoriatic erythroderma which for eight weeks had failed to respond to the usual treatment measures. Peroral administration of undecylenic acid made the condition decidedly worse. In this case, too, there was striking improvement after ACTH therapy. All lesions disappeared in one week. The patient did not have arthritis.

DR. ASHTON L. WELSH, Cincinnati: My associates and I have treated 2 patients who have acute disseminate lupus erythematosus with ACTH. Both were extremely ill—near death. Both became fever-free and greatly improved in two to three days. One, an 11 year old child, was removed from the hospital by the parents after five days' treatment. The child died of a cerebral hemorrhage

three days later. The other, a 28 year old woman had relapses on three occasions when administration of the drug was discontinued.

DR. JAMES H. MITCHELL: This is not a discussion on the subject, but it has to do with the use of ACTH in mycosis fungoides. According to information given me by Dr. Samuel Taylor, who has this drug for distribution, the case to which I refer is the first of mycosis fungoides that has been treated with the drug. The patient has been shown before this Society on a number of occasions. She had shown no pronounced improvement on sodium paraaminobenzoate therapy. She had three courses of nitrogen mustard but failed to respond to the third course. With ACTH she is still under treatment but has made surprising progress.

There were 9 patients with lymphoblastoma down East under treatment, but so far as we know the patient referred to is the only one with mycosis fungoides. One of the interesting manifestations of the treatment is the state of euphoria.

DR. F. T. BECKER, Duluth, Minn.: At the last meeting of the Minnesota Dermatological Society Dr. O'Leary stated that some of the patients under treatment with ACTH and cortisone acquired hirsutism and acne.

DR. HERBERT RATTNER: I have heard of a case in which a woman with lupus erythematosus had Cushing's syndrome after treatment with ACTH. Our little girl patient at Michael Reese Hospital also has changes suggestive of early Cushing's syndrome.

DR. JAMES R. WEBSTER: I can confirm Dr. Mitchell's observation of euphoria in some patients receiving ACTH. My associates and I were recently asked to see 2 Negro patients with advanced pulmonary tuberculosis who were receiving the preparation at Hines Hospital. One of these had become markedly exhilarated and the other slightly so.

They had both manifested a widespread follicular papular eruption on the face, trunk and extremities which was not acneform in character or distribution. Clinically we considered the folliclis type of papulonecrotic tuberculid, but histologically the lesions proved to be a nonspecific folliculitis which I assume was a direct result of the action of the hormone.

DR. S. J. ZAKON: We have at the present time a patient at Mount Sinai with acute disseminated lupus erythematosus. We were not able to obtain ACTH for her, and so we followed the suggestion of Dr. Stephen Rothman and treated the patient with filtered roentgen ray irradiation of the ovaries. After the third roentgen ray treatment there was rapid improvement, with the result that the patient is now in a period of remission.

DR. FREDERICK R. SCHMIDT: I discussed the case that Dr. Reihl mentioned with him last evening. I asked him whether his patient had had any transfusions, and he said yes. This point brings to mind the only person I have ever seen recover from a bona fide case of lupus erythematosus. This patient, a Chilean, was at the point of death. She received two blood transfusions, and it developed that she was a person with Rh-negative blood who then received Rh-positive blood. After the second injection, at a time when antibodies had been formed and fourteen days after the first transfusion, she went into extreme shock, so badly that hope was given up. She managed to survive, after which development she made a complete recovery. That event was one and a half years ago. I hear from her every once in a while, and she is in a good state of health. I am now trying to reproduce this reaction in women with Rh-negative blood who have lupus erythematosus. I should like to ask the members, when they run across a person with acute lupus erythematosus, to be sure to ascertain the state of the Rh factor.

DR. H. RODIN, South Bend, Ind.: At the Rochester meeting a case of subacute disseminated lupus erythematosus was presented in which a remission had been produced by the administration of testosterone propionate. Remissions in similar cases have also been reported following roentgen sterilization in the female and more recently through the use of ACTH. It appears that the androgenic steroids may provide the mechanism producing these remissions.

In the case presented at the County Hospital a biopsy of the testes revealed atrophy, and one may assume a decrease in the secretion of androgenic substance. It would seem that further investigation along this line is indicated.

DR. M. R. CARO: When the patient at Illinois was seen on October 14 the face lesions were ulcerated, but today they are almost entirely healed. My associates and I thought that ulceration in lupus erythematosus was sufficiently uncommon to make the case worth presenting.

As to the history of the bullous eruption that appeared right after the delivery of the baby, I am not sure that it was lupus erythematosus. The history makes me feel that it might have been a bullous toxic eruption.

DR. THEODORE CORNBLEET: Acute and subacute lupus erythematosus occurs so much more frequently in the female that that fact has suggested to many an endocrinal basis for this disease. All of us have seen this malady in males, too, as seen in my patient, so that all one can say is that feminine terrain is more suitable for whatever the pathogenesis may be. The patient today and another man have both been shown to have testicular atrophy. It is sheer speculation as to whether this gonadal change helped to make them subject to subacute disseminated lupus erythematosus or was produced by the latter. In both subjects the 17-ketosteroids have been quantitatively characteristic for women. Neither man has received much benefit from the use of testosterone, except for some improvement in well-being and strength. The lesions changed little, and the course of the disease has not been altered appreciably.

In contrast to the happy result in the woman who was said to have been temporarily sterilized with roentgen rays, I have seen this procedure fail. We are all praying that the good reports current from several sectors where ACTH and cortisone have been used in lupus erythematosus and in the so-called collagen diseases are ushering in a new era—that we shall be able effectively to control these disorders instead of having to stand by almost helplessly so often.

Congenital Telangiectasia (Rendu-Osler-Weber Syndrome?). Presented by DR. JAMES WEBSTER and (by invitation) DR. FRANCIS HETREED and DR. ALFRED B. FALK.

Hereditary Hemorrhagic Telangiectasia. Presented by DR. M. H. EBERT and (by invitation) DR. J. W. GRAFFIN.

G. W., aged 80, has had numerous skin lesions since childhood associated with frequent nosebleeds. Gastrointestinal bleeding has also occurred, and a diagnosis of bleeding peptic ulcer was made at one time. His mother had similar lesions on the tongue and nosebleeds. He has 4 children—2 boys and 2 girls—with the same condition.

He presents numerous telangiectatic lesions on the tongue, face and trunk. The red blood cell count varied between 3,000,000 and 4,600,000. The white blood cell count was 5,000.

Treatment has recently consisted of oral administrate of rutin, 10 mg. three times daily.

DISCUSSION

DR. F. T. BECKER, Duluth, Minn.: I agree with the diagnosis in the first case. In the second case I was very suspicious that the condition was a pulsating type of telangiectasia as seen with hepatic insufficiency.

DR. JAMES R. WEBSTER: We presented the young girl (the first case) as having a case of congenital telangiectasia because she has had it since birth. A history of other members of the family with the same disorder is lacking, and the girl has shown no hemorrhagic diathesis during her lifetime. Therefore, we felt it did not fit with the complete description of Rendu-Osler-Weber syndrome and should not be presented as such because loose grouping of cases under a handy name leads to confusion.

There is one other thing which we feel is interesting but probably not significant. Largely as a placebo we gave the patient ascorbic acid. She had never had any fading of the lesions prior to this measure, but we are all convinced, the patient and her parents as well, that these lesions are fading. I do not know why. The blood is completely normal as to clotting time. I think the patient is getting better, whether because of or in spite of ascorbic acid therapy, I do not know.

DR. M. H. EBERT: The only thing I know about the second case is that I think it is a true example of the Rendu-Osler-Weber disease. The patient has a history over at the Central Free Dispensary about an inch and a half thick. He has been in every department usually for hemorrhage from one organ or another. I do not see how the man keeps alive. I do not think the condition has anything to do with liver trouble. The patient has had it since childhood, and other members of the family have had the same thing.

Mycosis Fungoides? Presented by DR. EDWARD A. OLIVER and Staff.

A Case for Diagnosis: Lymphoblastoma? Insect Bite Granuloma? Presented by DR. EDWARD A. OLIVER and STAFF.

DISCUSSION OF PRECEDING TWO CASES

DR. S. M. BLUEFARB: The first case was presented for two reasons. First, when the woman was first seen in 1945 a diagnosis of parapsoriasis was made. A biopsy at that time verified the diagnosis. However, nodular lesions have developed lately and a recent biopsy disclosed a typical histologic picture of mycosis fungoides. The second point is the association of mycosis fungoides with malignant changes. This patient had a carcinoma of the cervix. If I may judge from a brief survey of the literature pertaining to the association of malignant changes and mycosis fungoides, this combination would appear to be an unusual observation.

The second case we thought very interesting although we are still doubtful as to the diagnosis. We are familiar with the work of Dr. Allen regarding insect bites as a cause of granuloma (*Am. J. Path.* **24**:367 [March] 1948). However, he emphasized the presence of eosinophils and plasma cells, and in our case these cells were not found. Since we are in doubt as to the classification of this case we have tentatively called it an infectious granuloma.

DR. M. R. CARO: Concerning the second case, I recently saw a patient with a lesion that was clinically identical and in whom the histopathologic picture was the same. My diagnosis in both cases is histiocytoma cutis.

Mycosis Fungoides. Presented by DR. M. H. EBERT and (by invitation) DR. V. LEAF and DR. D. MUSGRAVE.

DISCUSSION

DR. F. J. SZYMANSKI (by invitation): Examination of the cellular imprint made from a typical tumor of mycosis fungoides revealed the cellular components of normal blood. However, there was one cell slightly larger than the others, showing a nucleus with reticulated, closely interwoven, dark-staining chromatin and a small amount of basophilic cytoplasm. This cell puzzled us. Therefore, we called on Dr. Limarzi, the hematologist of the University of Illinois, who expressed the opinion that the cell in question was an undifferentiated blast cell. Reviewing the article written by Dr. Winer in 1947 in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**56**:480 [Oct.] 1947), we discovered a photograph of the same cell, and it was labeled a malignant reticulum cell. Dr. Winer concluded that the malignant reticulum cell is synonymous with the mycotic cell seen on histologic section. We were not able to verify that conclusion.

Extensive Nevus Pigmentosus et Pilosus. Presented by DR. F. E. SENEAR and STAFF.

Congenital Ichthyosiform Erythroderma. Presented by DR. STEPHEN ROTHMAN and DR. JOHN C. MURPHY (by invitation).

Extensive Nevus Unius Lateris. Presented by DR. FRED V. HAUSER (by invitation).

Darier's Disease. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. L. MARSHAK and DR. A. L. LORINCZ.

DISCUSSION OF PRECEDING FOUR CASES

DR. S. W. BECKER: The patient in the first case has an extensive nevus, which is quite rare. In this instance there was a negative familial history. Such a nevus is significant for two reasons. In the first place, such an extensive nevus is often associated with similar growths in the nervous system. As you know, there are normal melanoblasts about the medulla in normal persons, but in persons who have these extensive pigmented nevi, sometimes as infants or small children, there are mental symptoms which have been caused either by benign tumors in the central nervous system or by melanoma in the same organ. Melanoma occurs not too infrequently in this type of patient, even in childhood.

The second consideration, of course, is the cosmetic result of any sort of treatment. A person who has a lesion of this type is obviously embarrassed. Treatment has been carried out, preferably before puberty, by means of excision and plastic surgery, with sometimes pretty fair results.

The fourth patient, I thought, has ichthyosis. The spiny lesions at the anterior axillary line are typical of ichthyosis of the type which is associated with congenital hyperkeratosis, which this patient shows on the feet.

DR. ARTHUR C. CURTIS, Ann Arbor, Mich.: The lesions in the third case are so unilateral that it looks as though a plumb line had been dropped down from the chin. Not long ago a patient of mine had a lesion very much like this one on the neck and shoulders. The patient was treated by a plastic surgeon by means of sandpaper destruction, with the use of local anesthesia. The entire area of the nevus unius lateris epithelialized, and the scarring was minimal.

DR. JAMES R. WEBSTER: My remarks concern the case of pigmented hairy nevus. I wonder, in cases that are as extensive and noticeable as this, whether one is really justified in undertaking treatment. The results of treatment can be

considered only as relatively slight improvement, and the treatment itself cannot be regarded as entirely safe.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to endorse what Dr. Becker said about the fourth case. This is a universally distributed eruption of small follicular papules. Second, the microscopic changes are not those associated with Darier's disease. There are some minor dyskeratoses that one might expect in any type of ichthyosis. Most of them are fairly well localized. I think this child has an unusual ichthyosis.

DR. FRED T. BECKER, Duluth, Minn.: In the treatment of some of the keratodermas and ichthyosiform eruptions we usually give high doses of vitamin A. At a recent meeting of the American Roentgen Ray Society in Cincinnati Dr. Kaffey described cases of vitamin A poisoning. These all occurred in children, in whom the symptoms were anorexia, loss of weight and joint pain, especially over the tibia and ulna. Roentgenologically he found a periosteal reaction such as one would see in prenatal syphilis. The symptoms cleared up after treatment with vitamin A was stopped. I had never heard of vitamin A intoxication before.

DR. THEODORE CORNBLEET: Those patients who were described by Dr. Fred Becker as having had unhappy results following the use of vitamin A were all young infants, mostly premature babies. The vitamin A was administered in water-dispersed preparations. It is being vigorously denied, however, that the vitamin A was at fault in even these few cases.

If Dr. Rothman's patient has indeed Darier's disease it is of a peculiar distribution and arrangement which might be accounted for by her very young age. After puberty, when the sebaceopilary stimulation takes place, there may be a shift to seborrheic sites.

DR. A. M. BUCHHOLZ: About three years ago I had as patients identical twins with congenital ichthyosiform erythroderma. Vitamin A was administered to 1, and the other was used as a control and received none. The patient receiving vitamin A showed pronounced improvement. When its administration was stopped the child had a recurrence. Later we placed both children on treatment with vitamin A, and the control then also had clearing. I understand the children, who are now 4 years of age, are free from lesions. It may have been spontaneous clearing, but it would be well if any of you could try vitamin A to see whether these observations are valid.

DR. STEPHEN ROTHMAN: I was aware that the case has features which are rather atypical for Darier's disease, and I should have shown it as a "case for diagnosis." However, I cannot accept the diagnosis either of ichthyosis vulgaris or of congenital ichthyosiform erythroderma. This condition is a congenital keratinization anomaly which clinically and histologically most resembles Darier's disease.

Widespread Lichen Nitidus. Presented by DR. H. RATTNER and (by invitation) DR. H. RODIN and DR. S. Barsky.

Lichen Planus with Involvement of Face and Nails in Child Aged 8. Presented by DR. D. OMENS and (by invitation) DR. H. OMENS and DR. S. BARSKY.

Multiple Benign Cystic Epithelioma. Presented by DR. H. RATTNER and (by invitation) DR. H. RODIN and DR. D. MUSGRAVE.

Pronounced Improvement after Treatment with Bacitracin Ointment in a Patient with Seborrheic Eczema and Sycosis Barbae. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. SCHORR and DR. D. MUSGRAVE.

Chronic Lymphedema with Verrucous Dermatitis of the Toes. Presented by DR. F. E. SENEAR and Staff.

Lichenoid Toxic Eruption (Due to Chronic Ingestion of Quinine?). Presented by DR. STEPHEN ROTHMAN and DR. JOHN C. MURPHY (by invitation).

Base Squamous Cell Epithelioma of the Toe. Presented by DR. ROBERT C. RANQUIST (by invitation).

Huge Pedunculated Squamous Cell Epithelioma of the Back of the Neck. Presented by Dr. D. Omens and (by invitation) Dr. H. Omens and Dr. S. Barsky.

Chronic Lymphatic Leukemia and Kaposi's Sarcoma in the Same Patient. Presented by Dr. Theodore Cornbleet and (by invitation) Dr. D. Cohen and Dr. D. Musgrave.

Lepromatous Leprosy: Improvement from Treatment with Diasone.® Presented by Dr. Theodore Cornbleet and (by invitation) Dr. D. Cohen and Dr. D. Musgrave.

DETROIT DERMATOLOGICAL SOCIETY

Frank Stiles, M.D., *President*

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Oct. 19, 1949

All cases were presented by Dr. Loren W. Shaffer and the Staff of the Department of Dermatology, City of Detroit Receiving Hospital.

Lupus Erythematosus Treated with Paraaminosalicylic Acid: Five Cases.

L. S., a Negro aged 43, when first seen presented a circumscribed lesion on the upper lip which had been present since June 1946. There was an edematous plaque with elevated infiltrated borders and a scaly center with evidence of atrophy. The diagnosis was discoid lupus erythematosus and was confirmed by biopsy. Under treatment with bismuth sodium triglycollamate (bistrimate®) and gold sodium thiomalate (myochrysine®) during 1948 and 1949 there was gradual enlargement of the lesion. On April 8, 1949, treatment with paraaminosalicylic acid (pamisy®) by mouth was started and the amount gradually increased to 14.4 Gm. daily in four doses. Since Sept. 19, 1949, the patient has been maintained on a daily dose of 12 Gm.

J. S., a 39 year old white man, was first seen May 6, 1949, when he complained of generalized aches and pains and loss of strength. He presented an erythematous eruption in butterfly pattern on the face, lesions in and behind both ears, a large acute, infiltrated plaque on the back and several small lesions on the left arm. The facial lesions had been present for about a year but the more acute lesions for only a few days. Diagnosis, confirmed by biopsy, was lupus erythematosus disseminatus. The patient was advised to rest and protect himself from the sun. Paraaminosalicylic acid therapy was started and the dose rapidly increased to 14.4 Gm. daily. This treatment resulted in almost complete involution of the lesion by June 17, 1949, when the patient was lost from sight. He returned August 5 with a relapse which also involved the scalp, both shoulders, the chest and the arms. He stated that he had been taking sun baths hoping to improve his general condition. His temperature was normal most of the time, and the results of laboratory examinations were within normal limits. He was again started on paraaminosalicylic acid therapy and soon after began complaining of rather severe abdominal cramps, nausea and vomiting. These have continued although treatment was stopped Sept. 28, 1949.

B. N., a 35 year old white woman, had been ill with aches, fever and malaise for the past two years. She first noticed an eruption on her chin in May 1949. Skin lesions and systemic symptoms gradually became worse. She was admitted to Receiving Hospital Sept. 1, 1949, with an erythematous eruption on the face, neck, chest and arms. The lesions were circumscribed and rather infiltrated. The temperature ranged between normal and 102 F. The sedimentation rate was 46 mm. in one hour, and the white blood cell count, between 6,000 and 9,500. The diagnosis was lupus erythematosus disseminatus, which

was confirmed by biopsy. The patient was treated with rest, administration of multiple vitamins and paraaminosalicylic acid therapy, which was started Oct. 7, 1949, with a dose of 1.2 Gm. four times a day.

T. E., a 39 year old white woman, presented an erythematous crusted butterfly type lesion on the cheeks across the bridge of the nose when she was first seen by us, Sept. 7, 1949. After removal of the crust follicular plugging and some atrophy were apparent. The facial lesions had been present from three to four years, with improvement at times but never complete healing. The diagnosis was discoid lupus erythematosus and was confirmed by biopsy. Under treatment with paraaminosalicylic acid, up to 1.8 Gm. four times a day, there has been some improvement.

R. H., a 39 year old Negro woman, was first seen by us on Aug. 5, 1949. She presented several localized lesions on the face which showed hyperpigmentation, keratotic plugging and atrophy. There were also scattered erythematous, slightly scaly lesions on the extensor surfaces of both forearms and some denuded areas on the palms and tips of the fingers that gave the impression of having been bullae. The lesions on the face had been present for four years, but the one on the right cheek and those on arms and hands had occurred only two to three weeks previous to admission. The temperature ranged between normal and 102 F. A diagnosis of discoid and disseminated lupus erythematosus was made and confirmed by biopsy. Treatment has consisted in rest and the administration of paraaminosalicylic acid up to 9.6 Gm. daily.

Generalized Scleroderma Treated with Paraaminosalicylic Acid.

R. L. B., a 29 year old Negro woman, was first seen by us March 30, 1949, at which time her face was drawn and expressionless. She could open her mouth only with difficulty. The joints of her hands were somewhat flexed and to a great extent immobile. The skin was hard, inelastic and "hide bound" and could not be pinched. There were areas of depigmentation on both forearms. The present condition had started with what the patient thought to have been arthritis in her fingers in 1947 and had progressively grown worse. Roentgenologic examination showed osteoporosis of the bones of hands and feet and some pointing of the distal ends of the phalanges. There was suggestive evidence of involvement of the upper part of the gastrointestinal tract, particularly the esophagus. Treatment was started with paraaminosalicylic acid on April 15, 1949. The patient now takes 14.4 Gm. daily and uses petrolatum and hydrous wool fat locally.

DISCUSSION OF CASES OF TREATMENT WITH PARAAMINOSALICYLIC ACID

DR. OWEN S. HENDREN (by invitation): Paraaminosalicylic acid, which has been known as PAS for short, has been widely used for the treatment of tuberculosis both alone and in conjunction with streptomycin. In the Department of Dermatology, City of Detroit Receiving Hospital, we now have 10 patients under treatment with paraaminosalicylic acid. To date our maximum dosage has been 15 Gm. daily given in four divided doses. To date the only toxic manifestations we have encountered have been some gastrointestinal irritation such as nausea, vomiting and diarrhea. This has been controlled for the most part by the administration of aluminum hydroxide suspension; however, the dose has had to be reduced in a few patients and then gradually increased until the maximum amount was tolerated. In no case has there been any evidence of blood or kidney disturbances. At the present time paraaminosalicylic acid is being used in these conditions purely on an experimental basis and it is entirely too early to make any prognosis as to the eventual outcome.

DR. FRANK STILES: All patients seem to agree they had rapid improvement.

DR. ARTHUR SCHILLER: I disagree with Dr. Stiles. I questioned the patients, and they said that they improved up to a point and then suffered relapses while still under treatment. It may be that relapses can be prevented when more is known about proper dosage.

DR. CHESTER DOTY: If cleared by paraaminosalicylic acid once will the lesions remain healed, or will the administration of the drug have to be kept up?

DR. LEE CARRICK: I have a patient under treatment with paraaminosalicylic acid, 7 grains (0.42 Gm.) daily. The diagnosis was periarteritis nodosa, confirmed by biopsy. There has been about 75 per cent improvement after two weeks of paraaminosalicylic acid therapy.

DR. OWEN S. HENDREN: At the present time one patient with discoid lupus erythematosus has shown more benefit from treatment with paraaminosalicylic acid than from that with two other previously used drugs. The scar tissue is soft and noncontractile. There is still some activity about the border; however, the extension has been arrested.

In this series of cases are several patients that were placed under treatment while in the hospital with an acute or subacute dissemination. Up to this time none of these had another flare; however, as previously stated, it is still too early to know with any degree of certainty what influence this drug will have on lupus erythematosus and also on generalized scleroderma. I plan to continue the study with this group of patients for at least another six months, and by that time perhaps a few of the questions that are in all our minds may be partially answered.

DR. CHESTER DOTY: The patient with scleroderma states that her condition is much better since starting treatment with the drug.

DR. LOREN SHAFFER: Paraaminosalicylic acid is making a favorable impression at our hands. It is seemingly much less toxic than paraaminobenzoic acid. Nausea is fairly frequent in the larger dose range, and occasionally vomiting and diarrhea. The drug has not been in use long enough or in enough cases for one to appraise adequately its effectiveness in lupus erythematosus or related degenerative collagen disease.

Mycosis Fungoides Treated with Urethane.

S. S., a white man 54 years of age, presented a generalized erythematous eruption when first seen by us on Nov. 29, 1948. The dorsa of the hands had a purplish cast with lichenification. Lesions had been present for one month. During the next few months all the lesions assumed a more violaceous color, with thickening and lichenification of the skin. Pruritus became severer all the time. On Feb. 4, 1949, a nodular infiltrate was noticed on the back of the neck; more nodules developed soon after. The diagnosis of mycosis fungoides was confirmed by biopsy. The differential blood count showed 80 per cent neutrophils, 13 per cent lymphocytes, 5 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The patient had had the right leg amputated in 1937 and the left leg in 1945, both for Buerger's disease.

Treatment with urethane, 2 Gm. daily, was started on Feb. 23, 1949, and the dose was increased to 4 Gm. daily on March 29, 1949. On August 15 the daily dose was again reduced to 2 Gm. A rather severe keratosis-pilaris-like condition which involved arms and back was first noticed May 10, 1948. This has cleared up almost completely under treatment with daily doses of 100,000 units of vitamin A and the addition of mixed vitamins to the diet. The severe

pruritus was not relieved until after the patient had taken urethane for approximately four months. At present the skin presents an almost normal condition except for hyperpigmentation.

Mycosis Fungoides Treated with Urethane.

A white man presented a pruritic eruption of four years' duration. At first the lesions would regress under local treatment, but on admission in June 1949 the patient had generalized hyperpigmentation and lichenification of the skin and severe pruritus. A biopsy was reported as compatible with mycosis fungoides.

The patient was placed on treatment with three doses of 1 Gm. of urethane a day on July 16, 1949, and 1 per cent salicylic acid in petrolatum was applied to the skin. The pruritus improved six days later, and ten days after the institution of this therapy the lesions began to undergo involution. The patient was discharged from the hospital in good condition on Sept. 13, 1949.

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR. LOREN SHAFFER: Both of these patients made rather spectacular responses to urethane therapy. S. S. has been under treatment for eight months. He had typical patchy dermatitis at the start and several infiltrated beginning granulomatous lesions on the back, the largest and most typical being on the back of the neck. The pruritus was very severe. Clinical improvement was rapid, and the erythema and infiltration had largely disappeared by the end of one month. In spite of this clinical improvement very severe pruritus persisted to the point that the patient threatened suicide. Because of this fact roentgen ray therapy was considered, but before it was started the itching improved and by the end of the fourth month had largely disappeared. This patient has now had a total of 550 Gm. of urethane without recognized toxic effects.

DR. HARTHER KEIM: The case of S. S. looked like atypical pityriasis rosea until the infiltrated plaques appeared. The histologic examination showed lymphoblastoma. In the second case I could not be sure of the diagnosis today. All the patient shows is pigmentation. What was the clinical picture in the beginning?

DR. JAMES ROGIN: I have seen both patients from the beginning of their skin trouble. I saw the second man one year ago; then generalized erythroderma developed from what looked most like a diffuse atopic dermatitis. Biopsy showed mycosis fungoides.

DR. H. H. HOLMAN: When this patient was admitted to the Veterans Hospital the over-all picture was one of generalized neurodermatitis. The presence, in addition, of unusually deep pigmentation, extreme pruritus and an infiltrated plaque just above the right buttock led us to suspect lymphoblastoma. This suspicion was borne out by biopsy. The patient's condition has improved in a remarkable manner since the institution of urethane therapy.

Dermatofibrosarcoma Protuberans of the Thigh.

C., an obese light-colored Negro woman aged 49, has a nodular tumor on the anteromedial aspect of the left thigh. The lesion is reddish, measures 5 by 3 by 4 cm. and is composed of several confluent protuberances. The skin over it is thin and shiny, with dilated blood vessels. The tumor is firm around the edges and fairly soft in the center. The skin for a distance of 2 cm. around the base of the tumor is indurated, and infiltration extends into the subcutaneous panniculus.

The patient first noticed a small area of redness in this region nine years ago. This has grown, at first slowly and more rapidly in the past year. Recently there has been bleeding, and this was serious enough to cause the patient to seek medical assistance. There has never been any pain or other symptoms. The patient was first seen by us Oct. 18, 1949, and no biopsy has been taken as yet.

DISCUSSION

DR. COLEMAN MOPPER (by invitation): Although this case was seen for the first time today by the Dermatology Staff, we unhesitatingly made a diagnosis of dermatofibrosarcoma protuberans. At the City of Detroit Receiving Hospital within the past several months 2 cases of dermatofibrosarcoma protuberans located on the lower part of the back, both in obese Negro women, have been seen and these 2 cases will be reported (Mopper, C., and Pinkus, H.: Dermatofibrosarcoma Protuberans, *Am. J. Clin. Path.* **20:** 171 [Feb.] 1950). These tumors were clearly differentiated from other sarcomas by J. Darier (*Ann. de dermat. et syph.* **5:** 545-562, 1924), but tumors which were probably of the same nature had been described much earlier. A. Hertzler (*Ann. Surg.* **84:** 489-496, 1926) emphasized the non-malignant characteristics of these tumors and stated that metastases are very rare and that wide local excision is usually curative. Even in the presence of metastasis, however, a radical lymph node dissection is of great benefit, and no deaths were reported in his series. He also reported a case in which the patient was operated on seven times for such a neoplasm and was well some twenty years later.

E. Hoffman (*Dermat. Ztschr.* **43:** 1-28, 1925) pointed out that these cases are not as rare as the literature would indicate. They are usually seen by general surgeons, who, struck by the appearance of clinical malignancy, excise the tumor, and the routine pathologic diagnosis of fibrosarcoma overemphasizes the degree of malignancy. H. E. Michelson (ARCH. DERMAT. & SYPH. **25:** 1127, 1932) reported that he received three different reports from pathologists on the some tumor of this nature. We decided to report our 2 cases in a journal of pathology rather than in the dermatologic literature because we believed it was more important to call this tumor to the attention of general pathologists. Dermopathologists and dermatologists are much more familiar with it, and a proper pathological diagnosis is very important from a prognostic viewpoint.

DR. HERMANN PINKUS: It is a peculiar coincidence that 3 cases of this type, all in Negro women, should have been seen within a few months while no patients with the disorder had been admitted to Receiving Hospital for a number of years.

DR. ARTHUR SCHILLER: The lesion is quite vascular. Are these tumors of vascular origin?

DR. HERMANN PINKUS: The histologic picture can be described best as being between that of a fibroma and that of a fibrosarcoma. The predominant cell is a spindle cell, and the proportion of cells and intercellular connective tissue can vary widely in the same tumor. There are usually but few mitoses. The number of blood vessels usually is not more than average, and vascular origin is not likely. It appears important to recognize this type of lesion clearly because of the great difference in prognosis between it and true spindle cell sarcoma.

DR. CHESTER SIDELL: In 1 case with which I am familiar the tumor was excised and recurred repeatedly over twenty years. It remained localized.

DR. THOMAS MILLER: What is considered typical of the clinical aspect?

DR. COLEMAN MOPPER: The lesion is definitely infiltrated into the subcutaneous tissue and is quite firm, whereas the elevated portion has definite protuberances at the periphery and was probably formed by small nodules which coalesce to produce this large tumor or by outgrowths from other nodules. This is a fairly characteristic picture. In addition, in the present case the skin overlying the tumor was thin, and I am certain that in time this tumor would ulcerate and a red, vegetating mass would project through the opening. I am certain the histologic picture will confirm our clinical impression.

NOTE.—Subsequent biopsy and histologic examination confirmed the diagnosis of dermatofibrosarcoma protuberans.

BRONX DERMATOLOGICAL SOCIETY

Charles R. Rein, *Vice President, in the Chair*
Henry Silver, M.D., *Secretary*
Oct. 20, 1949

Long Remission in Mycosis Fungoides Treated with Antimonials. Presented by DR. JOHN GARB.

D. N., a woman aged 49, was presented before the Bronx Dermatological Society on Oct. 23, 1947, and reported on in the *Journal of Investigative Dermatology* (**10**:43, 1948). She had generalized lesions of over eight years' duration, consisting of extensive infiltrated patches, numerous ulcerations and tumorous growths.

From April 24, 1947, until Jan. 13, 1949, she received 10 intramuscular injections of antimony potassium tartrate (5 cc. of 1 per cent solution), 73 intramuscular injections of 4 cc. of stibanose® (the diethylaminoethanol salt of sodium antimony gluconate) and 58 of stibophen (fuadin®) at twice weekly intervals. The total amount of antimony used was 8.48 Gm.

Except for having minor electrocardiographic changes (the antimony treatments were suspended during the time these were observed), the patient has been in good health and had no subjective complaints.

The only local therapy used was podophyllin (resin of podophyllum N. F.), 1 to 2.5 per cent solution in compound tincture of benzoin; it was applied to the persisting infiltrated patches on the right leg.

At present the patient presents one patch the size of a 25 cent piece on the left buttock.

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR. FRANK E. CROSS: I should like to ask Dr. Garb to give us a summary not only of the three cases, in which the results are truly remarkable and significant, but also of the entire series of his cases to date.

DR. RUDOLF L. BAER: The old standby, arsenic, has been much used in mycosis fungoides, but I am in doubt as to whether such relatively complete, long-lasting remissions have occurred. Pharmacologically, antimony and arsenic are closely related. I should like to ask the members of the Society who have had experience with arsenic in treatment of mycosis fungoides whether such long remissions have been observed.

DR. MAX JESSNER: In my experience, the treatment of mycosis fungoides with arsenic preparations combined with roentgen ray therapy was almost always followed by long periods of remission. I recall one case in which the remission was of several years' duration and the patient died ultimately of cancer of the rectum. I would not hesitate to give arsenic and roentgen rays in doses above the usually accepted amount. Mycosis fungoides is regarded as a fatal disease, but patients may live for decades with it, and it is immaterial whether they get arsenical keratoses or other by-effects.

I may point out that Dr. Garb's first patients treated with antimony potassium tartrate showed astonishing results, but later on a number of other patients did not respond as well.

DR. FRANK E. CROSS: My results with a small number of cases treated with antimony potassium tartrate were not so favorable; rather, the condition was definitely made worse, and in one patient, who had been given a small dose, there developed convulsions and exfoliative dermatitis. Are not some of the reactions to antimony potassium tartrate too severe? Is the drug worth using in view of the severe reactions?

DR. DAVID BLOOM: From my personal observation of several patients and particularly of one in the tumor stage of mycosis fungoides I have the impression that antimony is a valuable additional drug in the treatment of the disease.

DR. NATHAN SOBEL: Concerning the toxicity of antimony, I have supervised over 500 cases of granuloma inguinale in which this drug was used over long periods and have encountered relatively few reactions; those obtained were relatively minor.

DR. LOUIS CHARGIN: Taken by and large, the results obtained by Dr. Garb with antimony potassium tartrate must be regarded as highly satisfactory. If 3 patients out of 12 have been made comfortable for a period of nine months or longer, then much has been accomplished. Nevertheless, the last word concerning the effect of this drug in mycosis fungoides has not been said.

DR. CHARLES WOLF: In comparing antimony to arsenic, I believe that arsenic is a greater protoplasmic poison to the individual cell. We should, therefore, avoid the use of arsenic and prefer antimony as the less toxic drug. Other forms of treatment have been temporarily successful, such as, for example, roentgen irradiation. I have seen rapid disappearance of 30 to 40 disseminated tumors following roentgen ray therapy. On the other hand, while treated tumors regressed, new tumors would appear. The great advantage in Dr. Garb's treatment is that individual lesions melt away and no new lesions appear during treatment.

DR. JOHN GARB: I have never seen satisfactory results from the use of arsenic in mycosis fungoides. The patient in case 1 received so much arsenic that she became toxic. In addition, she had several courses of roentgen ray treatments which affected the hemopoietic system. The tumors and ulcerations became generalized so that ordinarily her life expectancy could not have been more than a few months. In three weeks, after 10 injections of antimony potassium tartrate, she showed a striking improvement.

Of the three antimony preparations I consider antimony potassium tartrate first, stibophen second and stibanose® last in effectiveness. I recommend 20 intravenous injections of a 1 per cent solution of antimony potassium tartrate given three times weekly, treatment to be continued with stibophen or stibanose® until all lesions have healed and to be followed by weekly injections of stibophen or stibanose® for six months.

Patients with mycosis fungoides who respond to antimonials will manifest pronounced improvement within three to six weeks. If a noticeable betterment is not obvious during that period, antimonials will probably be of little help.

The untoward reactions are arthritic pains, usually in the shoulders, eruptions, tachycardia, bradycardia and other myocardial changes. These changes are usually reversible within six weeks after treatment with the antimony preparation has been discontinued. A hemogram, electrocardiogram and a liver function test should therefore be carried out about once a month to prevent grave complications.

I have presented three out of 10 patients treated successfully with antimonials at the Skin and Cancer Unit. The other seven patients should not be used as a criterion of the effectiveness of antimony in mycosis fungoides; two could not continue treatment because of myocardial damage; in one there developed sclerosed veins; one with extensive ulcerations and tumors refused further treatment because of pains in the wounds after two injections, and one died of intestinal obstruction, probably due to a tumorous growth. It has been my experience that cases with extensive ulcerations and tumorous growths of long standing appear to respond best.

Primary Hodgkin's Disease of the Scalp. Presented by DR. JULIUS H. POLLOCK.

M. G., a man aged 59, was seen at the Department of Dermatology of the New York University–Bellevue Medical Center on Sept. 16, 1949, presenting a swelling on the right side of the scalp and neck which had been present for the past five months. The past history is irrelevant.

The tumor on the scalp consisted of three firm, slightly elevated reddish to coppery lesions. They were sharply demarcated, somewhat scaly and nontender. At the angle of the jaw there was a moderately enlarged lymph node.

Examination of the blood on July 27, 1949, showed 4,600,000 red cells, 14.5 per cent hemoglobin and 4,300 white cells with 67 per cent polymorphonuclear cells, 25 per cent lymphocytes, 3 per cent eosinophils and 5 per cent monocytes. The Wassermann reaction of the blood was negative.

Histologic examination by Dr. C. Miller on July 20, 1949, showed the middle part of the lower third of the cutis occupied by one large cellular mass. The cells were wandering lymphocytes, connective tissue cells, white blood cells and large clear cells with vesicular nuclei; the last-mentioned were multinucleated, suggesting Dorothy Reed cells. There was a loose connective tissue stroma about the mass.

Shortly after the second biopsy was performed a pronounced diminution in size, elevation and appearance of the lesions occurred. Similarly the gland on the right side of the neck has considerably diminished in size, to that of a lima bean.

DISCUSSION

DR. ALEXANDER A. FISHER: Is there any history of an insect bite? Occasionally such bites show a histologic picture of Hodgkin's disease.

DR. CHARLES WOLF: I recall the case Dr. Greenhouse presented at this Society many years ago. The lesions in this case, however, are small. Primary Hodgkin's disease of the skin is rare. In Hodgkin's disease there is usually a primary focus elsewhere than in the skin. I am inclined to believe that the case presented is not primary Hodgkin's disease of the skin.

DR. CHARLES A. GREENHOUSE: At the time we presented our case there had been about 55 cases of primary Hodgkin's disease reported in the literature (ARCH. DERMAT. & SYPH. **29**:569, 1934). Dr. Pollock's case and ours had a number of

similar features. The ages of the patients were the same; the lesions were on the scalp in both cases; the pathologic features were identical, and both cases responded to treatment.

Clinically, our case resembled a gumma; the pathologic findings were recognized as suggestive of Hodgkin's disease by Dr. P. Klemperer and by Dr. D. L. Satenstein. I am of the opinion that primary Hodgkin's disease of the skin is not as serious a disorder as we have been led to believe.

DR. WILBERT SACHS: I should like to cite a relevant case of an elderly woman with a lesion on the hand. Dr. Satenstein and I made the diagnosis of Hodgkin's disease on histologic examination. After a thorough physical examination no evidence of Hodgkin's disease was found. Two or three years later the patient died of Hodgkin's disease.

DR. MAX JESSNER: Cases of primary Hodgkin's disease of the skin are known but are extremely rare. The French speak of a "chancre lymphogranulomateux." But there is still some controversy about this point because it is practically impossible to be sure whether or not some deep lymph node has been affected before. At the time I was a young assistant, I observed just such a case, which was later published by W. Doessekker (*Archiv. Dermat. u. Syph.* **126**:596, 1919). That case also started with a tumor on the scalp. It was impossible to make a definite diagnosis either clinically or histologically. One year afterward the disease spread on the scalp and over the body, but even from these lesions it was not possible to diagnose Hodgkin's disease with certainty. Afterward, the glands became swollen, and the patient died several years later of generalized Hodgkin's disease confirmed by autopsy.

In the case shown tonight the diagnosis is doubtful because the lesion has disappeared and a definite histologic interpretation was not possible.

DR. JULIUS H. POLLOCK: On purely clinical grounds I was unable to make the diagnosis of Hodgkin's disease. The histologic changes suggest the possibility of Hodgkin's disease but are not sufficiently definite to warrant an unequivocal diagnosis. Another unusual feature is the disappearance of the tumors about four to five weeks after onset. Drs. Greenhouse and Cornell observed their case of primary Hodgkin's disease of the scalp for a period of seven years, without the appearance of lesions elsewhere (Greenhouse, C. A.; and Cornell, V. H.: ARCH. DERMAT. & SYPH. **29**:569, 1934).

Scleredema Adultorum (Buschke). Presented by DR. FRANCES PASCHER.

M. S., a man aged 78, became aware of a "hardness" around the neck earlier in the summer. There was no history of any illness preceding the onset of the eruption. From 1935 to 1940 the patient had attacks of petit mal with loss of consciousness. After an injury in 1944 he had a rupture of the right biceps muscle. In 1945 he had grip lasting for three days.

The patient presents a hard edema involving the skin of the neck, the shoulders and the front and back of the chest. There is no change in color, no tenderness or alteration of sensation. The skin does not pit on pressure.

The patient has been treated with aureomycin orally since Sept. 8, 1949. He has received 250 mg. every four hours for two weeks and then 0.5 Gm. four times a day. There appeared to be some softening of the affected skin of the chest. The patient complains that loose stools and belching follow the ingestion of aureomycin.

The blood coagulation time on Sept. 29 was 6 minutes, 8 seconds; on Oct. 6, 6 minutes, 4 seconds, and on Oct. 13, 7 minutes, 5 seconds.

DISCUSSION

DR. PERRY M. SACHS: While in service in the United States Army, I treated a young man with widespread scleredema. After 1½ years' treatment with massage and physical therapy, improvement was not more than 25 per cent. This response was decidedly less rapid than that usually claimed.

DR. CHARLES R. REIN: With regard to by-effects of aureomycin, I have observed three patients in whom there developed a severe perianal dermatitis shortly after the administration of the drug. Has anyone had similar experience?

DR. ALEXANDER A. FISHER: Yes. I have observed two cases of perianal dermatitis following the administration of aureomycin.

DR. ELLEN REINER: I have observed erythema-multiforme-like eruptions and smoothness of the tongue following the use of aureomycin.

DR. DAVID BLOOM: In one case of scleredema adultorum injections of hyaluronidase softened the treated areas, but the softening lasted only a few days.

DR. FRANCES PASCHER: After treatment with aureomycin there has been some softening of the "hard" edema, but it is not striking—no more than one would expect in the natural course of the disease. Three determinations of the coagulation time were made in this case because the work of Macht showed that the coagulation time may be shortened considerably as a result of antibiotic therapy. He warned against the danger of thrombotic changes in the vessels. There was no alteration in the coagulation time in this case.

Angiokeratoma. Presented by DR. JOHN GARB.

L. S., a girl aged 15 years, registered at the Skin and Cancer Unit of the New York University–Bellevue Medical Center on Aug. 9, 1949, complaining of growths on the feet of nine years' duration. Her sister, aged 21, has no such lesions. There is no history of consanguinity or of a similar disturbance in near or distant relatives. The patient has no pain on walking, but the lesions bleed after scratching. There is no history of frostbite. The general health is good.

The eruption first appeared on the dorsal surface of the right second toe as bluish red spots the size of a pinhead. During the past five years new lesions developed on both feet and the older ones became larger and raised. During the past year purplish puncta appeared on the fingers.

The growths are located on the dorsal surfaces of all the toes, the distal half of the right foot, the great and little toes and the distal third of the left foot. On the plantar surfaces the growths are distributed mostly on the right great toe, outer surface of the remaining toes, and the heel and outer surface of the left foot at areas of greatest pressure and friction. The lesions consist of well defined soft, discrete, painless growths from pinhead to split pea in size, some of which coalesce, forming larger growths. On the inner surfaces of the middle joints of the ring and index fingers and on the outer surface of the right ring finger are located similar purplish puncta.

Inspection with the magnifying glass of some of the larger and more distinct growths reveals closely but evenly placed dark purplish angiomas the size of a pinhead. They project from the surface, especially from the periphery, imparting to the warty-like purplish base a glowing effect like amethyst. The growths on the feet are fairly easily compressible, but the color of these as well as of the puncta on the fingers is not in the slightest altered on diascopic pressure. The feet and hands appear to be of normal moisture and temperature.

The routine laboratory tests showed no abnormalities. A section taken of a lesion of the right foot was examined by Dr. C. F. Sims. The cutis proper presented nothing of pathologic importance. In the papillary bodies dilated blood vessels were seen, some of which were engorged and thrombosed. The basal layer contained some pigment. The epidermis was irregularly acanthotic and verrucous. There was considerable hypergranulosis and hyperkeratosis. The histologic diagnosis was angiokeratoma.

DISCUSSION

DR. DAVID B. BALLIN: I have seen three cases of this disease, and it strikes me that they were all in Italians. Since the original case was described by Mibelli I wonder whether it is coincidental that all these patients were of Italian descent. Has anyone seen the disease in other than Italians?

DR. MAX JESSNER: These cases are extremely rare. I do not remember having seen such an excellent example of the disease before.

DR. NATHAN SOBEL: There is another type of angiokeratoma that occurs on the scrotum. This has been named the Fordyce type of angiokeratoma. In a patient under my observation some years ago, the entire scrotum was covered with lesions.

DR. DAVID BLOOM: This condition is due to a congenital weakness of the blood vessels which may or may not lead to angiokeratoma. There is frequently an association of chilblains in the patient himself and in other members of the family, or there may be a varicocele or varicosities of the legs.

DR. JOHN GARB: There is no history of consanguinity in my case and no pain on walking. Most of the lesions are at points of pressure and friction. I believe that the growths might subside on relief of the pressure at the areas involved.

Leprosy Resembling Livedo Reticularis. Presented by DR. NATHAN SOBEL and (by invitation) DR. MABEL G. SILVERBERG.

Leprosy Resembling Sarcoid or Secondary Syphilis. Presented by DR. NATHAN SOBEL and (by invitation) DR. MABEL G. SILVERBERG.

Mycosis Fungoides with Many Lesions Resembling Fixed Eruption. Presented by DR. LOUIS CHARGIN.

Epidermolysis Bullosa Dystrophica; Consanguinity of Parents. Presented by DR. DAVID BLOOM.

A Case for Diagnosis: Toxic Bullous Eruption? Pemphigus Vulgaris? Treatment with Aureomycin. Presented by DR. FRANCES PASCHER.

Parapsoriasis Varioliformis. Presented by DR. LOUIS CHARGIN.

Lichen-Planus-Like Eruption Following Gold Therapy. Presented by DR. ELLEN REINER.

Angiofibroma. Presented by DR. CHARLES F. SIMS and DR. JOHN GARB.

Leukoderma Acquisitum Centrifugum in Siblings. Presented by DR. JOHN GARB.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Captain Robert L. Gilman (MC), U.S.N., *Chairman*

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Oct. 21, 1949

Congenital Ichthyosiform Erythroderma. Presented by DR. JOHN P. SCULLY, Reading, Pa.

R. H., a white woman aged 30 years, soon after birth acquired a bullous eruption on an erythrodermic background. The bullous lesions had lessened by the end of her first year. She has had persistent dryness and scaling of the skin during

her lifetime. During the past summer recurrent pruritic erythematous lesions of the lower extremities were secondarily infected at times.

The blood count, sedimentation rate, fasting blood sugar, results of urinalysis and blood urea nitrogen were normal. A hemolytic Staphylococcus aureus, coagulase-positive, was cultured from the leg.

The biopsy report was as follows: "The epidermis was moderately and densely hyperkeratotic. The rest of the epidermis was acanthotic and highly edematous; Spongiosis was conspicuous at some places. The significant lesion was a thin vesicle or bleb which lay at the level of the stratum granulosum and extended barely to the stratum squamosum. It contained red blood cells and serum at some places, and everywhere there were shreds of degenerated epidermal cells within it. It was obvious that the liquefying processes were connected with a restricted stratum of cells in relation to the stratum granulosum. In fact, at the extreme edge of the bleb it was the cells of the stratum granulosum alone which were undergoing spongiotic processes.

"In the corium a considerable infiltration of edema appeared around the blood vessels, with only moderate inflammatory cell infiltration. A few plasma cells and eosinophils were intermixed with the lymphocytes. The walls of the vessels were thickened by edema.

"Inasmuch as the abnormalities centered so obviously within the region of the skin where the processes of keratinization are paramount, it will have to be conceded that ichthyosis is a logical diagnosis. However, the processes were most unusual in view of the liquefactive phenomena. I was perplexed by the fact that an abundance of fibrin occupied some parts of the vesicle, thus indicating an inflammatory factor. Moreover, some of the epithelial cells immediately underneath had dense, hyaloid cytoplasms suggestive of fibrinoid necrosis, and the Fuelgen reaction would be welcome to settle this point. In short, I was unable to affix a diagnosis, but dermatitis herpetiformis can be excluded."

The patient has been treated with vitamin A, 50,000 units three times daily, and the local application of equal parts of hydrous wool fat and aquaphor.®

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.: This case is 1 of a number occurring in eastern Berks County and western Lehigh County, in Pennsylvania. To give a typical case history, the disease appears shortly after birth; it has ichthyotic features which are more prominent in the winter months and symptoms of epidermolysis bullosa simplex which are more prominent during the hot weather. It is a dominant characteristic. In one family a mother and a daughter are affected. In another family the father, twins and another child are affected. A similar case was presented at the Atlantic Dermatological Conference in Montreal, and another from Lehigh County by Dr. Douglass Decker a few years ago. I do not know how they should be classified. They certainly do not fit in with the localized type of ichthyosiform erythroderma that was seen in Pittsburgh some years ago. I have shown 2 cases of that disorder at meetings of this Society, and they do not resemble the present case. I think, for want of a better diagnosis, we should label cases of this sort bullous ichthyosis. In the females affected there is usually an exacerbation at the time of their menstrual periods, which are often irregular and on the scanty side.

DR. A. STRAUSS: I think this is rather a recurrent type of dermatitis, according to the history the patient gave me. It becomes worse in summer and disappears in winter. I think this may be one of the type due to some pollens.

DR. MORRIS MARKOWITZ: As to "congenital" ichthyosis: If it does not affect the soles and palms, it is not congenital. In this case the soles are affected, and so I think the diagnosis "congenital" stands.

DR. LOUIS GOLDSTEIN: I have had 1 of these patients that Dr. Butterworth just mentioned under my care for a number of years. The only thing that seems to help him is the administration of diphenhydramine (benadryl®). It keeps the bullae under control. So there must be some allergic factor in these cases, not in the ichthyosis but in the process of formation.

Tinea Capitis in a 17 Year Old Soldier (Residual Infection?); Alopecia Areata Associated with Tinea Capitis? Presented by DR. LESLIE NICHOLAS.

J. M., a white youth aged 17 years, of normal appearance, including secondary sexual changes, presents an area of alopecia over the right occipital region; part of the area is completely bald, and the rest is covered with short, broken-off hairs. Along the neck line there are two areas of alopecia recently developed, one measuring 2 by 3 cm. in diameter, and the other, 1 by 1 cm. The original area, formerly 2 cm., is now 6 by 12 cm. Examination under the Wood light had positive results; in the two smaller areas there were several fluorescent hairs, while in the large area only three fluorescent hairs were seen.

The patient had "ringworm" of the scalp at the age of 12 years; it was treated with salve, and a small (about 2 cm.) area of alopecia remained. The 2 cm. area of alopecia remained unaltered from age 12 years until about the middle of August 1949, when the area suddenly enlarged.

Examination of a specimen prepared with potassium hydroxide solution revealed fungi. Culture showed Microsporon audouini.

The patient was treated with pragmatar® (a nonstaining ointment containing cetyl alcohol-coal tar distillate, 4 per cent; near colloidal sulfur, 3 per cent, and salicylic acid, 3 per cent, in a readily washable oil in water emulsion base) for two weeks while awaiting laboratory reports, without improvement. Zinc-undesal (salundek®) has been used since Oct. 5, 1949.

DISCUSSION

DR. D. M. SIDLICK: Having seen the patient for the first time tonight, I do not intend to question the diagnosis of tinea tonsurans. But I should like to ask Dr. Nickolas on what basis the diagnosis was made. Clinically it does not seem to be in consonance with the concept usually entertained for this condition.

DR. A. STRAUSS: I agree with Dr. Sidlick. Clinically I would say that it is a case of alopecia areata. The hairs regrowing do not look like the hairs that grow in tinea capitis.

DR. DOUGLASS A. DECKER, Allentown, Pa.: This boy has trichotillomania associated with tinea capitis. I asked him whether he pulled his hair, and he said, "No."

DR. JOHN P. SCULLY, Reading, Pa.: I am currently seeing high school children who came from grade school with tinea capitis now going on to their fifteenth and sixteenth year with M. audouini flourishing. I have 2 patients well beyond the middle of their fifteenth year, still with tinea capitis.

DR. LESLIE NICHOLAS: We need not argue about whether it is possible for tinea capitis to exist in the adult; we all know that it is. I presented this case, first, because I had never seen anything like it before and, secondly, because I

wanted to know what to do with the patient. I want to be able to tell the Army whether to keep him as a soldier or to return him to civilian life. Is it safe to keep this soldier in barracks with 10 other soldiers? Will he spread the disease? I do not know the answers. As far as the diagnosis is concerned he told me on the first visit three weeks ago that he had a patch of ringworm when he was 12 years old and that he had a residual patch of alopecia which just recently suddenly spread. When I examined him, half of the area was completely bald and the other half was covered with short, broken-off hair. The broken-off hair did not fluoresce. The fluorescent hairs were in the periphery. That point is in agreement with Dr. Decker's suggestion of trichotillomania. I do not know whether the patient has alopecia areata or tinea. Whichever it is, I think is immaterial. The important thing is that he still has some tinea capitis, and I should like to know whether anyone can help me as to this man's disposition in the Army.

(The consensus was that it would be safe to allow this man to remain in the Army.)

Malignant Melanoma. Presented by DR. MEYER L. NIEDELMAN.

W. P., a white man aged 25 years, had a black, flat, nonhairy mole about ⅛ inch (0.32 cm.) in diameter on the left shoulder, posteriorly, for many years. In June 1949 it suddenly began to grow. It has a tendency to bleed on even the slightest friction. It has not been irritated or traumatized. It is now a circumscribed, elevated, black mass about ½ inch (1.27 cm.) in diameter and ⅜ inch (0.96 cm.) above the surface. The periphery is coal black and the center somewhat lighter, with a rough surface. To the left of the lesion and at its periphery are two brown nevi. There is no adenopathy, infiltration or satellite lesions.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.; We have all made mistakes in cases of this type, but I think Dr. Niedelman is making it in the right direction. When we obtain a history of a mole's having suddenly taken on growth and an appearance such as this tonight, we all immediately think that the condition is a malignant melanoma. Then we excise it widely and the pathologist reports granuloma telangiectaticum. I think that diagnosis should be considered in this case. The patient has a very friable lesion with a dark crust and has had a hemorrhage from the lesion almost every day. What shall we do with it? If it is granuloma telangiectaticum we can clear it up with roentgen rays or fulgurate and desiccate the base and get a good result. If it is melanoma, however, it will be too late to cut out the base.

DR. REUBEN FRIEDMAN: A few intramuscular injections of crysticillin® (procaine penicillin G for aqueous injection), 600,000 units, should produce great improvement in the course of a few days if the lesion is granuloma telangiectaticum.

DR. VAUGHN C. GARNER: My thought with regard to this patient would be to remove the lesion in toto with wide, circular excision and examine it histologically. The lesion is on the upper part of the back; the scar will be of no cosmetic importance to a young man of his age, and I think he should be given the benefit of the doubt that this lesion is highly malignant. If it is malignant melanoma, treatment may be too late, but even so it seems to me that wide surgical excision will allow us to arrive at a diagnosis. If the lesion is not melanoma, the excision will do the patient no harm.

NOTE.—Three days later the entire lesion, with a ½ inch border of normal skin, was excised by electrosurgery. The histologic diagnosis made at Temple University Medical School was malignant melanoma. An extensive resection of the previously excised area was performed by the surgical department. At the time of writing (January 1950) the patient had no evident adenopathy or recurrence.

Mycosis Fungoides. Presented by DR. WILLIAM J. CAMPBELL (by invitation) for DR. EDWARD F. CORSON.

A. C., a white woman aged 59 years, presents a variety of cutaneous manifestations. On the midportion of the face, extending from the glabella to the upper lip and from midcheek to midcheek, is an area of red, irregular, hypertrophic granulation tissue completely obscuring the normal configuration of the face. The surface is grossly irregular. The right naris is completly occluded and the left naris partially occluded by the process. The conjunctivas are injected, and threads of mucopurulent material extend across the palpebral fissures. Large, pink, scaly plaques with rather distinct margins are found on the buttocks, the abdomen, the medial surface of the right arm and the right elbow. On the back are two lesions forming incomplete circles. On the chest is a purplish red, deeply indurated, partially healed lesion. Apparently the patient has been in good health except for red, nonelevated spots on both cheeks, forearms and on the trunk which began about eighteen years ago. Six years ago she acquired a severe sunburn, as a result of which large papules developed across her nose, cheeks and forehead. Much edema and erythema developed, and the lesions coalesced. Since 1947, shortly after the death of her husband, the lesion began to grow and has continued increasing in size until the present.

A complete blood count revealed 12 Gm. of hemoglobin, 4,290,000 erythrocytes, 7,100 leukocytes, 54 per cent segmented polymorphonuclear leukocytes, 51 per cent neutrophils, 12 per cent small lymphocytes, 32 per cent eosinophils and 5 per cent monocytes. The results of spinal fluid examination were within normal limits. The fasting blood sugar was 100.2 mg. per 100 cc.; the blood calcium, 10.0 mg. per 100 cc., and the blood phosphorus, 4.1 mg.

Dr. Beerman's pathologic diagnosis was mycosis fungoides. Previous pathologic diagnoses were lupus vulgaris and lupus erythematosus.

The patient has been treated with streptomycin, pencillin, roentgen rays, nitrogen mustard and gold preparations.

DISCUSSION

DR. MEYER L. NIEDELMAN: Has chaulmoogra oil been tried? Dr. O'Leary has reported that chaulmoogra oil given intramuscularly daily and the use of the hypertherm® apparatus may be of some value in retarding the process.

DR. HARVEY BLANK: A drug with an action somewhat like nitrogen mustard is urethane, which can be given simply by mouth in doses of 3 or 4 Gm. a day. Occasionally one sees dramatic results of its use in lymphoblastomas. There is a case reported (ARCH. DERMAT. & SYPH. **60**:625 [Oct.] 1949) of a man with lymphatic leukemia and carcinoma of the skin which showed rather striking temporary improvement under treatment with urethane. It is not a difficult form of therapy and is without much danger, if the blood picture is watched.

DR. JAMES M. FLOOD, Sayre, Pa.: Last year in Chicago I talked with a man who had had some success in treating 1 case of mycosis fungoides with 2 per cent podophyllin ointment. It might be useful to paint some podophyllin on this lesion.

Urticaria Pigmentosa. Presented by DR. EVAN B. HUME.

J. F., a white woman aged 42 years, presents widespread brownish macules which flare and wheal when stroked. There are many telangiectases on the face, with multiple spider nevi on the V of the neck. There are two large spider nevi on the left thigh. The lesions were first noticed on the back at the age of 31, and then they spread to the chest and extremities.

The patient is being treated for a pelvic disorder.

A biopsy was performed by Dr. Isaac Pels of Baltimore in 1946.

DISCUSSION

DR. EVAN B. HUME: I should like some help in this case. This patient is from upstate, and Dr. Pels told her some years ago that there was not much that could be done for her. I am of the same opinion, but I should like to know whether anyone has any suggestions to offer. Particularly, what is the effect of antihistaminic drugs in these cases?

DR. JOHN F. WILSON: The only thing I can add, from my experience with 1 case, is that after much antihistaminic therapy there is no change.

Epidermolysis Bullosa with Destruction of Hands. Presented by DR. WILLIAM J. CAMPBELL (by invitation) for DR. EDWARD F. CORSON.

J. C., a white man aged 29 years, thin and in poor physical condition, presents many scars of previous bullous lesions. Stumps are all that remain of the hands. Atrophy of tissues is pronounced. Since infancy the patient has had trouble with his skin. After incidental trauma the skin would be easily scarred. Vesicles and bullae are quite common, especially in hot weather. Exacerbations and remissions are common. The patient's parents are living and well. He has a sister with the same condition. There is no diabetes, cancer or tuberculosis in the family history.

A blood count revealed 70 per cent hemoglobin (11.5 Gm.), 3,500,000 erythrocytes and 6,200 leukocytes. The serologic tests for syphilis gave negative reactions.

DISCUSSION

DR. VAUGHN C. GARNER: I have had a patient with a similar case under my care for twenty-odd years; I saw him first when he was 3 years of age; he is now 26 and just recently—in the past week—has had to be subjected to amputation in the midarm because of the development of malignant changes on his epidermolysis bullosa. I have followed this young man in my private practice and have observed changes almost identical with those seen in the patient tonight. His terminal phalanges are gone. He has this multiplicity of scars and atrophy over the body, and about a year ago he acquired squamous cell carcinoma of the forearm. Dr. Pfahler kept the condition under control by intensive roentgen ray therapy for some months, but finally it got ahead of him and he asked consultation from a man in New York; it was the joint opinion of Dr. Pfahler and this New York consultant that the boy should be subjected to amputation. I mention this case merely because it is the exact counterpart of the one presented tonight and it is the only case in my experience in which the ultimate result is a squamous cell carcinoma.

DR. JOHN F. WILSON: I saw Dr. Garner's patient last week, just after his arm was removed, and looked through the literature but was unable to find a similar case of a squamous cell carcinoma in epidermolysis bullosa. I think it interesting that he gave a history of being a drummer.

Favus, Probably Contracted in China. Presented by CAPTAIN ROBERT L. GILMAN (MC), U.S.N.

S. G., a white man aged 23 years, presents an atrophic, erythematous, scarring alopecia of the vertex and sides of the scalp. On admission the posterior portion of the scalp was covered with a heavy yellow crust. Anteriorly there were cup-shaped yellow crusts. There are several round, pigmented, crusted lesions and scars, 1 cm. in diameter, on both legs. The patient also has tinea versicolor on the chest.

The dermatitis had its onset on the scalp and legs in China, in 1946. It was "healed" for a period of six months after roentgen ray epilation of the scalp in 1947. On Oct. 11, 1949, cultures were made and Trichophyton schoenleini was recovered.

The patient has had no previous cutaneous trouble. He has never been in Europe. There is no history of favus in the family. Both his parents were born in Italy. He has been married a year; his wife is unaffected.

The patient has been treated with undecylenic acid ointment and fitted with a toupee.

A Case for Diagnosis: Atypical Keratosis Pilaris? Presented by DR. THOMAS BUTTERWORTH, Reading, Pa., and (by invitation) DR. F. P. COOMBS.

M. M., a white girl aged 17 years, well developed and well nourished, presents a follicular erythematous punctate eruption over the back and shoulders. Each follicle involved contains keratinous material and is surrounded by a red halo. The condition is asymptomatic, and there is no seasonal change. The patient, an epileptic imbecile, had pneumonia at 3 months of age. Her mental peculiarity was noted at this time. She had chickenpox at the age of 1 year, and whooping cough and mumps, at 2. There is no history of syphilis. Her mother and father are living and well. She has 1 brother, living and well and mentally normal. A paternal uncle is speechless and totally deaf. The girl was admitted to an institution for feebleminded persons in 1940, and the eruption on the back was recorded then.

A complete blood count, results of urinalysis and blood sugar determination were within normal limits. The serologic tests for syphilis gave negative reactions.

Report on the Biopsy.—The diagnosis was follicular keratosis with granulomatous reaction (rule out tuberculid). This section presented very little that was outstanding except for a mild lymphocytic inflammatory reaction and a single giant cell around a single hair follicle and moderate hyperkeratosis, particularly around the hair follicle (Dr. Herman Beerman).

The patient has been treated with vitamin A 200,000 units every day (after a meal) for over ten months, with no improvement; with vitamin A similarly administered plus 200,000 units given intramuscularly every week for three months, with some improvement; with ultraviolet radiation, with no improvement; with occlusive dressings, with no improvement, and with sulfur and salicylic acid ointment, with no improvement.

A Case for Diagnosis: Atypical Keratosis Pilaris? Presented by DR. THOMAS BUTTERWORTH, Reading, Pa., and (by invitation) DR. F. P. COOMBS.

S. L., an overweight white woman aged 25 years, with some tremor, presents a diffuse follicular keratotic erythematous punctate eruption over the back and shoulders. It is asymptomatic, with no noticeable seasonal change. The patient

is an epileptic imbecile of Mongolian appearance. She has had the eruption on her back since 1931. Her mother is mentally deficient and epileptic. She has a sister in the State Hospital.

A complete blood count, results of urinalysis and blood sugar determination were within normal limits. The serologic tests for syphilis gave negative reactions.

Report on the Biopsy.—The diagnosis was mild follicular keratosis and dermatitis. The epidermis showed some irregularities of the surface with mild hyperkeratosis. The basal layer was intact. There was a slight perivascular and peripilosebaceous lymphocytic infiltration. The sweat glands and subcutaneous fat were normal (Dr. Herman Beerman).

The patient has been treated with the vitamin B complex, 2 tablets three times daily; solu-B® (a sterile powder containing thiamine hydrochloride, 10 mg.; riboflavin, 10 mg.; pyridoxine hydrochloride, 5 mg.; calcium pantothenate, 50 mg., and nicotinamide, 250 mg.) 1 cc. intramuscularly weekly, and the application of wool fat, occlusive dressings and sulfur and salicylic acid ointments, with no improvement.

A Case for Diagnosis: Atypical Keratosis Pilaris? Presented by Dr. Thomas Butterwotrh, Reading, Pa., and (by invitation) Dr. F. P. Coombs.

W. V. F., a white woman aged 26 years, imbecile to moron, presents over the back and shoulders a keratotic follicular punctate eruption which has been present since 1931. It is asymptomatic with no noticeable seasonal change. The patient's mother has syphilis; 1 sister is mentally deficient, and the patient has congenital syphilis. She has suggestive Hutchinsonian teeth.

A complete blood count, results of urinalysis and the amount of blood sugar were within normal limits. The serologic tests for syphilis gave negative reactions.

Report on the Biopsy.—The diagnosis was follicular keratosis (mild dermatitis). These sections of skin revealed slight hyperkeratosis with keratotic plugging of follicular orifices in a rare focus. There was mild acanthosis and focal perivascular and lymphocytic cuffing. The sections were otherwise not remarkable.

The patient has been treated with 200,000 units of vitamin A daily, by mouth; 200,000 units of vitamin A once weekly, intramuscularly; the vitamin B complex, 2 tablets three times daily; solu-B®, 1 cc. weekly, and the application of sulfur and salicylic acid ointment, with no improvement.

DISCUSSION

Dr. Reuben Friedman: Why is the condition not a punctate seborrheic dermatitis?

Dr. Thomas Butterworth, Reading, Pa.: We have about 9 of these cases at the institution. I do not think 9 cases out of 2,500 would warrant any conclusion as to an association between this condition and feeblemindedness. Most of the eruptions are limited to the posterior surface of the trunk. Changes in the usual areas involved in keratosis pilaris are rather minor or nonexistent. On the theory that the condition might be follicular seborrheic dermatitis, these patients have been treated with sulfur, salicylic acid, ammoniated mercury and tars. To eliminate any factor in the coarse garments worn in the institution, we have applied occlusive dressings of hydrous wool fat over large areas of the back to see whether it made any differnce, and it has not. This summer Dr. Coombs did a large number of biopsies and furnished them to Beerman. The histologic observations were consistent with keratosis pilaris. All the preparations we have tried have produced no improvement. In the years that I have been following

this particular type of case, I have seen only 1 of this type in private practice, although I have seen many typical cases of keratosis pilaris. I think this type is atypical in location and lacks the acuminate characteristics.

DR. F. P. COOMBS (by invitation): The pathologic picture seems to be quite consistent with keratosis pilaris, but, clinically, the absence of lesions in the usual distribution and the absence of association with ichthyosis are against that diagnosis. I checked the literature for the possibility of the condition's being lichen pilaris or lichen scrofulosorum, but the cases presented have been persistent over a long time and without the rather acute onset. In the majority of that group the prognosis is fairly good.

The eruption seems to be definitely confined to the back without any evidence of lesions in the typical areas. Brocq in 1890, in the *Annales de dermatologie et de syphiligraphie*, reviewed the literature, and from what I could gather there were no cases reported of the disorder's being on the back without some involvement of the arms.

DR. HERMAN BEERMAN: We studied these sections carefully, and there was very little in them to account for the appearance that we saw tonight. Does Dr. Blank think these are like the follicular lesions seen in the Negro children at the Children's Hospital?

DR. HAREVY BLANK: They are similar. The distribution and lack of histologic evidence in this case would tend to make one consider the diagnosis of an atypical keratosis pilaris. Certainly it is difficult to compare the peculiar follicular disease that Negro children have with other cutaneous diseases. The minimal histologic changes found in it are similar to those in the cases presented.